

ADRENAL CORTICAL RESPONSES TO STRESS IN NORMAL MEN  
AND IN THOSE WITH PERSONALITY DISORDERS<sup>1</sup>

## PART I. SOME STRESS RESPONSES IN NORMAL AND PSYCHOTIC SUBJECTS

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## INTRODUCTION

Because the work we are about to report represents the cooperative efforts of persons representing several disciplines it has seemed to us fitting, before presenting our data, to say a few words about the particular orientation—philosophy, if you will—upon which our studies are based.

Santayana in his "Scepticism and Animal Faith" wrote: "Scientific psychology is a part of physics, or the study of nature; it is the record of how animals act. Literary psychology is the art of imagining how they feel and think."

To physiologists and biochemists concerned with problems of human behavior certain basic working assumptions are implicit. Man is an animal despite his complexity and, as such, is a part of nature and subject to study by procedures that have repeatedly proved their use in the physical sciences and in biology which, of course, includes the medical sciences. The concept of a disembodied psyche independent of bodily processes can no longer warrant serious consideration. Thus all behavior, from the knee jerk reflex to the appreciation of Beethoven's Ninth Symphony, is regarded as the interplay of subtle physicochemical

mechanisms which are analyzable, given sufficiently developed scientific disciplines—a condition not realized in 1949. Differences between two samples of so-called normal behavior, in the same situation involving let us say one's self and one's neighbor, involve differences in adjustment mechanisms in the nervous system and elsewhere in the body. These differences are the resultant of previous conditionings acting through a substratum furnished by the genes which set limits to our capacities and to our modes of responding. This point of view is of course not unique but is also tacit in the assumptions of most investigators of psychological phenomena.

Psychotic patients—schizophrenics to be more specific—display differences in behavior which distinguish them as a diagnostic group from the rest of us, and just as surely as their distorted thought processes and affectivity set them as a group apart from us we believe that the physiological and chemical substratum of these differences, which certainly must exist, is a worthy subject of investigation. Schizophrenia is, we thus believe, an "organic" disease no less than is any other. By this we mean that the schizophrenic process must certainly involve aberrant physicochemical events. The failure of science in 1949 to have demonstrated satisfactorily this organic basis should be neither surprising nor especially discouraging to investigators.

Of course the study of individual human behavior, both normal and abnormal, is a study in psychosomatic relations. Our position is that mental processes and their physiological concomitants are two sides of the same coin, and it is folly to emphasize the ultimate triumph of one over the other. Both the psychological and physiological disciplines have much to contribute to understanding behavior, normal and abnormal.

<sup>1</sup> Read at the 105th annual meeting of The American Psychiatric Association, Montreal, Quebec, May 23-27, 1949.

This and the following four papers constituted a symposium on Psychosomatic Relationships in Personality Disturbances.

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New concepts of mechanisms are now available involving negative feedback principles which are by definition *purposive, goal-directed mechanisms*. These mechanisms may possess memory and some also display learning. Such mechanisms are characterized by the properties of nerve nets, endocrine interrelations, and a variety of electronic man-made circuits(1, 2). These concepts further reduce to the realm of meaningless questions the mind-body problem from the point of view of the dualists and the German idealists, on the one hand, with their emphasis on the primacy of mind, as well as for the behaviorists, on the other, who deny its very existence(3).

In the studies about to be reported we have endeavored to correlate measured aspects of behavior with measured aspects of endocrine responsivity. Because of the nature both of our data and of our assumptions as just outlined, we have avoided the scientifically meaningless question of causality as presented in the traditional views of the "mind-body problem."

Since 1943 the staff of the Worcester Foundation for Experimental Biology, among other activities, has published 24 papers dealing with stress responses of the adrenal cortex.<sup>4</sup> Of these papers, 7 have been animal studies, 8 have been investigations of normal men, and 9 are studies of psychotic patients in comparison to normal controls. Of the 24 papers only 3 have appeared in a journal devoted to psychiatric matters; the rest were published for the most part in the physiological literature. We therefore believe that a brief résumé to this

<sup>4</sup> This work has been carried out by a group of investigators at the Worcester Foundation working in collaboration with the research staff of the Worcester State Hospital. The Foundation group has consisted primarily of Harry Freeman, Fred Elmadjian, Louise Romanoff, David Stone, James Carlo, Victor Schenker, and the authors. Valuable cooperation over the years has been furnished by Roy G. Hoskins, William Malamud, Irene Malamud, Eliot Rodnick, Sidney Sands, Austin Berkeley, and David Shakow of the Hospital Staff. In addition, the work would not have been possible without the help of a number of technical assistants. Our work has been aided by the Office of Naval Research, the U. S. Public Health Service, the Williams-Waterman Fund of the Research Corporation, G. D. Searle & Company of Chicago, The Schering Corporation, Armour and Company, and Ciba Ltd.

association of psychiatrists of some of our published findings is in order before proceeding to discuss our recent results.

#### STRESS AND ADRENAL CORTICAL PHYSIOLOGY

The adrenal cortex has been intensively studied in the last two decades, and in this period approximately 2,000 papers have appeared dealing with its physiology and the chemistry of its hormones. Twenty-eight hormone-like substances have been obtained from it(4), all belonging to the class of compounds known as steroids, which are quite different chemically and pharmacologically from the single hormone epinephrine produced by the adrenal medulla. The steroids are four-ring carbon structures with characteristic short side chains, and having molecular weights around 300. The adrenal steroids belong to the same chemical family as the sex hormones. Of the 20-odd adrenal cortical substances some have not as yet been assigned any known physiological rôle, although the physiology of others is quite clear. Three of the adrenal cortex substances, for example, are primarily concerned with the conversion of protein to sugar and the storage of this potential fuel in the liver. Others regulate the salt and water balance in the body, particularly the balance of sodium and potassium between cells and body fluids, so essential to normal tissue function, including that of the brain.

Unlike the adrenal medulla, which is under direct nerve control, hormone release from the adrenal cortex is accelerated by a protein substance carried by the blood stream from the anterior pituitary. This adrenal-stimulating adrenocorticotrophic hormone as it is called, hereafter referred to as ACTH, is discharged from the pituitary by the nervous system by mechanisms that are still obscure(5, 6). The control of ACTH is also regulated, in part, by the level of adrenal cortical hormones in the circulation so that the higher this level the less ACTH is released(6).

Considerable evidence, especially from animal studies, indicates that hormones from the adrenal cortex play a significant rôle when the organism encounters stressful situations. The work of Hans Selye and his collaborators in Montreal on the "alarm reac-

tion" has been especially illuminating, as have studies from the laboratories of C. N. H. Long of Yale and Dwight J. Ingle of the Upjohn Company. Animals forced to severe exercise, or exposed to low oxygen pressures to simulate high altitudes, or to extremes of cold, or to surgical injury, or to injections of toxic agents, show reversible anatomical changes in the adrenal cortex and reversible changes in its ascorbic acid and ester cholesterol content. Animals in which the pituitary has been removed do not show these adrenal changes with stress and those deprived of the adrenal cortex early display marked weakness and lassitude preceding collapse and death after a few days. These latter animals are very unresistant to stress of any kind. The syndrome of Addison's disease in man has long been known to be a destructive disease of the adrenal cortex. It is typically characterized, among other symptoms, by progressive lassitude, exhaustion, and ultimate death, and psychotic behavior in Addisonian patients is not uncommon. Animals deprived surgically of their adrenal cortices and Addisonian patients can be maintained in a healthy state by the administration of adrenal cortex hormones which serve as substitutes for the hormones normally produced by the gland. The interested reader is referred to a recent excellent review of adrenal cortical physiology by Noble(7).

#### INDICES OF ADRENAL CORTICAL FUNCTION IN MAN

At present there are a number of methods available for the assay of adrenal cortical function in man. Because of the far-reaching reverberations on metabolic processes produced by these hormones, various measures of blood and urinary constituents are delineative of the relative level of adrenal activity.

Thus certain specific adrenal steroids concerned with protein and carbohydrate metabolism have been shown by Dougherty and White(8) to produce a drop in the circulating lymphocytes. The protein of lymphoid tissue is in part converted to sugar which is then stored in the liver. Accompanying this protein breakdown uric acid appears in excess in the urine(9, 10). Recent work

from the laboratory of George Thorn(11) has shown decreases in circulating eosinophiles in response to the same adrenal hormones that depress the lymphocyte count.

Other adrenal steroids differing chemically only very slightly from those concerned with protein and sugar metabolism regulate the excretion of sodium and potassium so that changes of concentration of these salts in the urine are useful indices of the relative amounts of these circulating hormones in the same individual under experimental and control conditions(12).

The true adrenal steroids, in contrast to the steroidal sex hormones, have a side chain that has reducing properties. Measurements of total neutral reducing substances (the reducing lipids) in sugar-free urine represent, for the most part, certain forms of steroids of adrenal origin(13). In the course of chemical transformation in the body many, but by no means all, of the corticosteroids are converted to what are called 17-ketosteroids because they have an oxygen atom (keto group) on the number 17 carbon of the steroid skeleton. The 17-ketosteroids and reducing lipids may be analyzed in as little as an hour's collection of urine(14). In men 70%-90% of the 17-ketosteroids are of adrenal origin, the rest from the testes; in women probably 100% are derived from the adrenal cortex(4, 15).

In the stress studies to be described we have used 6 urinary and blood measures systematically to assay adrenal cortical function in man. There have been changes in the circulating lymphocytes and, in the urine, changes in 17-ketosteroids, neutral reducing lipids, potassium, sodium, and uric acid. Samples of blood and urine are taken before the stress from the resting fasted subject, an hour and 15 minutes later at the end of the stress, and at 2½ hours poststress.

Fig. 1 shows schematically how these indices reflect adrenal cortical function in relation to the relative activation of this organ.

#### BASAL VALUES FOR PRESTRESS INDICES

Table 1 presents data of prestress control values taken on 2 different occasions from groups of 34 schizophrenic patients and 36 normal men. The determinations were made



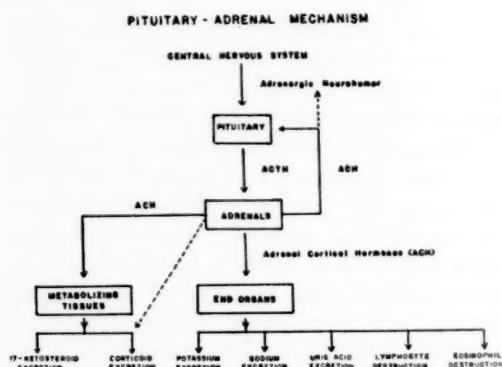


FIG. 1.—Evidence indicates that adrenocorticotrophin (ACTH) is released by a neurohumor from the hypothalamus. ACTH is the only known agent that accelerates the release of adrenal cortex hormones (ACH) over basal resting levels. Cortical hormones exert regulatory negative feed-back on the pituitary and perhaps on the central nervous system. Released ACH is metabolized in part to 17-ketosteroids and corticoids which appear in the urine. End organs are lymphoid tissue and also muscle and brain since sodium and potassium contents of muscle and brain are in part controlled by ACH. The kidney with its modification of excretory thresholds by steroids also belongs in the rectangle labeled end organs.

have imbibed more freely before coming to the tests than did the controls. These data do, however, suggest that the patients may be somewhat hypoadrenal, a view consistent with their small lipid excretion and large sodium excretion. The basal pattern of excretion in the patients is thus not much different from that of the controls. In all our urinary analyses creatinine is determined, and because of its constant rate of excretion it serves as a measure of reliability of our collections as discussed in our earlier papers. We shall return later to a comparison of the effects of stresses on these adrenal indices in the 2 groups after first reviewing some of our earlier stress response data.

#### REVIEW OF OUR EARLIER STUDIES OF STRESS RESPONSES IN MAN

During the war we studied fatigue of aviators and found that individual differences in fatigability of pilots were correlated with secretion of hormones from the adrenal cortex. In subsequent studies we found that

TABLE 1

MEAN BASAL VALUES AFTER 14 HOURS FASTING FOR CONTROL SUBJECTS AND SCHIZOPHRENIC PATIENTS (Two sets of determinations on each group. Italic numbers in the control group are different from those of the patient group to a 1% level of confidence by Fisher's *t* test)

	Urine volume cc./hr.	17-keto-steroids mg./hr.	Neutral reducing lipids mg./24 hrs.	Uric acid mg./min.	Potas- sium mg./min.	Sodium mg./hr.	Urinary PO <sub>4</sub> mg./min.	Creati- nine gm./24 hrs.
36 controls .....	66.4	0.50	3.02	0.48	191	237	0.59	1.80
34 patients .....	156.2	0.68	1.77	0.55	199	361	0.32	1.69
36 controls .....	61.2	0.38	3.00	0.50	157	193	0.55	1.68
34 patients .....	132.9	0.61	1.57	0.50	193	322	0.24	1.60

in the morning and no food had been taken since the previous evening. This table shows no significant differences between the 2 groups in 17-ketosteroid excretion, uric acid excretion, potassium excretion, or creatinine excretion. But differences reliable at the 1% level of confidence are found in the other measures as is indicated by the numbers in italics. The patients excrete less neutral reducing lipid material and considerably more sodium. Their urine volume output is, however, nearly twice as much as that of the controls, and this may account for the excessive sodium excretion since we did not control water intake and the patients may

a wide variety of common work-a-day stresses produced enhanced activity of this gland.

There are many patients in our mental hospitals who have notably failed to meet the stresses of daily life and have as a consequence developed bizarre and incapacitating behavior patterns, and we asked ourselves if it might be possible that these psychotic patients would show inadequacies in this very general stress response system. Just as the engineer tests the strength of structural materials by forcefully stressing them and measuring the strains, it seemed reasonable to stress psychotic patients and normal



people with the same standard procedures and compare their adrenal responses.

While it is true that everyone probably has a breaking threshold to the batterings of life, it is not true that schizophrenia is the necessary form of mental breakdown. Why some people develop a crippling psychosis with very little apparent stress and others do not, even in excessively stressful situations, is a challenging mystery the answer to which may ultimately lead to a rational form of chemotherapy.

Since 1941 we have made a number of studies of a variety of forms of stresses on normal men and women and on mental patients in relation to adrenal cortical physiology. During the first 3 years of this work urinary 17-ketosteroid assays were the only practical methods available for the analysis of adrenal cortical function in man. Since 1945 we have used in addition the number of circulating blood lymphocytes, and since 1946 changes in urinary sodium, potassium, uric acid, and the reducing lipids have also been used by us to elucidate adrenal activity. Our various studies have involved approximately 200 normal men and women (*i. e.*, persons with no known history of neuropsychiatric disorder) and 100 hospitalized mental patients, for the most part chronic male schizophrenics, although we also have data from a number of psychoneurotic patients and patients with involutional psychosis.

Our experimental stresses have included such patently physiological ones as exposures to heat(16), exposures to cold(17), and the ingestion of large doses of sugar(18-20). We have studied adrenal function before and after the psychomotor stress of prolonged fatiguing operation of a pursuit meter, a device simulating the operation of an airplane, with airplane-type controls requiring skilled coordinations in order to make good performance scores(21, 22). The pursuit meter has been used at sea level conditions and with the additional stress of having the operators breathe air low in oxygen to simulate high altitudes. In these experiments fatigue was measured by the rate of decline of performance scores and correlated with adrenal cortical activity. We have studied adrenal cortex function before, during, and after 152 training flights of 16

Army instructor pilots, and similar studies were made of 56 flights of 7 civilian test pilots(21).

On the purely psychological side we have studied adrenal cortical function in relation to psychological interviews, especially designed frustration tests, and examinations given to college students in regular course work(12, 21, 23). All these tests with the exception of this last and of the actual airplane flights of the pilots have been administered both to schizophrenic patients and to normal control groups. In normal people we have found these stresses to enhance adrenal cortical activity. We find that within limits the greater the stress the greater the adreno-cortical hormone output, and we have been able to correlate measured aspects of fatigability in the pursuit meter test from one man to another with his adrenal cortical secretion.

The schizophrenics as a group, in contrast, showed a striking inability to respond to our tests with enhanced steroid output as measured by our blood and urinary indices despite the fact that their resting 17-ketosteroid excretion was not different from that of the general population(23). As we have seen from Table I these patients have functional adrenal cortices and are not at all like Addisonian patients, but their adrenal cortices *on the average* are unresponsive to stress and unable to alter action with changing situational demands.

#### FURTHER EVIDENCE OF ADRENAL UNRESPONSIVITY IN SCHIZOPHRENICS— NEW STRESS DATA

The Rodnick-target-ball frustration test (24) has been described elsewhere. It is a game of skill requiring psychomotor coordination in which the subject is told what average and superior scoring ability generally achieves. In terms of these norms he is asked to set his own aspiration. This done he finds at first that he is able to make satisfactory scores. However, as time goes on, because of properties of the apparatus, and manipulations of the experimenter which are unknown to the subject, he finds himself unable to attain the aspiration level he set himself and thus becomes increasingly frustrated.

Figure 2 shows data from samples of blood and urine taken within 15 minutes after this test (the first of each pair of rectangles) and 2½ hours poststress (the second of each pair of rectangles) obtained from 36 control men and 20 male schizophrenic patients who had been without food for the preceding 14 hours. All values are relative and compared to prestress determi-

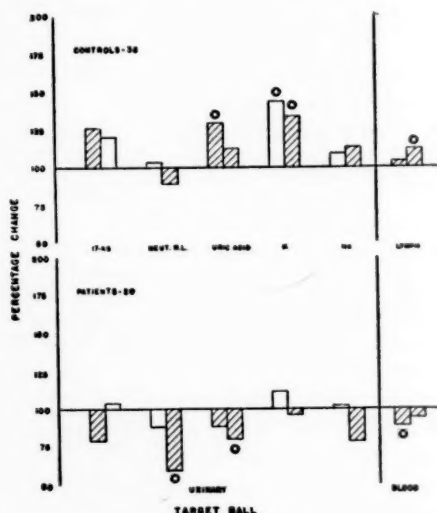


FIG. 2.—Target ball frustration test data from 36 controls and 20 schizophrenic patients who had fasted from the preceding evening. Comparison of 6 adrenal cortical indices are shown in percent changes from prestress levels. The first of each pair of rectangles is from urine or blood samples taken within 15 minutes of the termination of the hour stress. The second rectangle of each pair corresponds to samples taken 2½ hours poststress. Analysis of prestress samples always taken before the test furnished the base for the relative percent changes. Cross-hatching indicates statistically significant differences to at least the 5% level of confidence between patient and controls. Circles above the rectangles indicate this same level of confidence for changes from the prestress values.

nations of the 6 constituents obtained from prestress samples and assigned arbitrary values of 100. The prestress urine samples were ordinarily 2-hour collections made after rising in the morning. In this and in subsequent figures the cross-hatched rectangles signify values which, between the patient and control data, are significantly different to the 5% level of confidence or better by Fisher's *t* test. In most of the cases cross-hatching indicates significance at the 1%

level or better. Circles above the columns designate similar statistical reliability of differences between the immediate poststress and 2-hour poststress levels when they are compared to prestress values taken as 100. We see that there is an elevation of 17-ketosteroid output in the controls immediately after the stress and a fall in the case of the patients and that while the differences between patients and controls is significant these changes in this particular stress are not significantly different for 17-ketosteroids from the base line as indicated by the absences of circles above the rectangles. There is a significant drop in neutral reducing lipids of the patients in 2-hours poststress but the small drop in the controls is not in itself significant although the difference between patients and controls is significant. Uric acid excretion shows a significant rise for the controls after the stress and a significant decrease in the second poststress sample for the patients, and the differences between patients and controls are significant for both stress and poststress samples. Significant increases of potassium excretion is seen for the controls but not for the patients. Sodium excretion is affected in opposite direction for patients and controls at 2 hours poststress while lymphocytes average a rise in the controls and a fall in the case of the patients. Since this last result was opposite to what we had expected from earlier work it will be discussed later.

Judged subjectively a more effective psychomotor stress than the target ball test is our pursuit meter test described earlier. Data from 46 normal controls and 36 schizophrenic patients are presented in Fig. 3, and the differences of indices for the 2 groups is here sharply in contrast. The 17-ketosteroids show marked and significant rises in the controls and falls in the patients after the hour stress, but no significant differences between the 2 groups in their poststress neutral reducing lipid excretion are seen. Significant differences occur in the rises in uric acid, potassium, and sodium excretion of the controls and corresponding falls for these values in the patients. Again the lymphocytes in the patients show a significant fall while in the controls they display a slight poststress rise. We thus see changes in op-

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posite direction of our adrenal stress response indices in the 2 groups with the potassium index and 17-ketosteroid index showing especially striking differences.

Considering only the urinary indices the rises of the control values signal adrenal stress responses, but what about the declines in stress values for the patients? It is not at first apparent that adrenal cortical unresponsivity of the patients should produce lower stress values than their prestress values. The reason for this is due to the diurnal rhythm of secretion of the adrenal cortex which we have previously demonstrated (17, 21). There is a marked rise ( $50 \pm 14\%$ ) in adrenal cortical output in the first 2 hours after rising in the morning in normal persons and a lesser but still significant rise in schizophrenic patients. This is followed by a progressive decline during the day. Since the prestress samples (100%) therefore give higher indices we would expect that subjects who are nonresponsive to a stress given later in the morning would show poststress indices below the 100% level.

These pursuit meter stresses are actually a composite of 2 different types of pursuit meter tests divided about half and half between all of the subjects. In one set of observations the subjects were required to score for an hour continuously on the pursuit meter and in the other tests a pursuit meter embodying similar principles of operation was used but involving scoring for only one minute every other minute with rest intervals between. Elsewhere (23) we have broken down the data for these 2 types of operation and shown that our blood and urinary indices indicate that somewhat more stress is involved in the first 2 of these procedures. Figure 3, however, is a composite of all our pursuit meter data in this series.

In earlier studies we have reported a fall of lymphocytes in normal persons on stress and a predominant rise in the patients and this is just opposite to the results shown in Figs. 2 and 3. Thus Fig. 4 from an earlier publication (16) shows the relative change in poststress lymphocytes over prestress values taken as 100 for 11 normal subjects (closed circles) and 21 schizophrenic patients (open circles) when subjected to the severe physiological stress of exposure

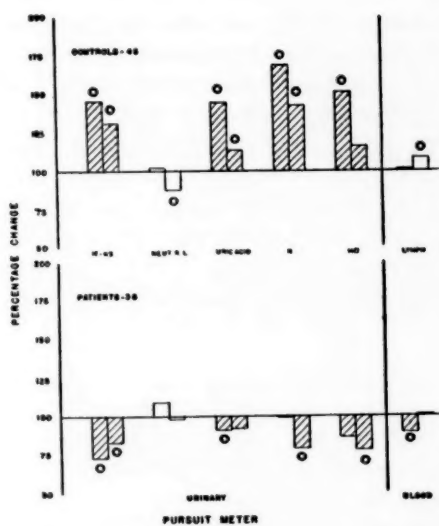


FIG. 3.—Comparisons of adrenal cortical stress response indices in pursuit meter tests for 46 fasting controls and 36 fasting schizophrenic patients. See text and legend to Fig. 2 for further description of this figure.

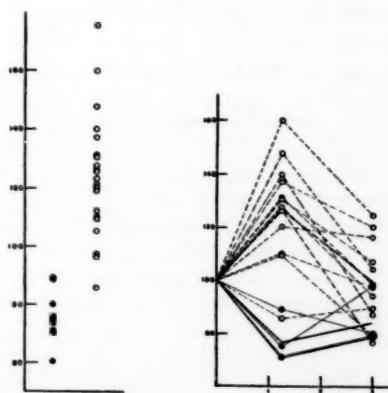


FIG. 4.—Left: Stress lymphocyte counts in 11 control subjects (closed circles) and 22 psychotic patients (open circles) as compared to prestress levels. The stress was exposure to high temperature and high humidity for an hour. For discussion, see text.

Right: Changes of relative lymphocyte counts with time in 4 normal subjects (solid lines) and 12 psychotic subjects (broken lines). The heavy solid and broken lines represent the mean percent values for controls and patients respectively. Abscissa time in hours; ordinate percent. [From Pincus and Elmadjian (10).]

for an hour to temperatures of  $105-112^{\circ}\text{F}$ . and 85% to 95% humidity. The patients are sharply separated from the controls by an average elevation of lymphocytes in contrast to



the decline for the controls. Similar lymphocyte changes have been found for stresses involving an hour's continuous pursuit meter operation combined with anoxia(22).

To account for the difference in lymphocyte behavior between our present results and those reported earlier we have proceeded as follows. In Part II of this paper a total response index (TRI) for adrenal stress responses is described. For the pur-

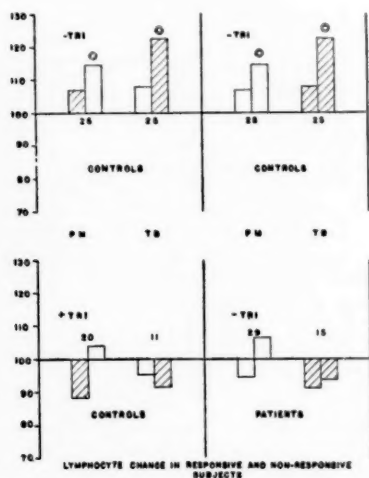


FIG. 5.—Comparison is made on the left half of this figure of lymphocyte behavior of normal controls who do (+ TRI) and who do not (— TRI) show significant *over-all* adrenal cortical responses to target ball and pursuit meter tests in terms of a measure involving all 6 of our indices. On the right half of the figure, similar comparison is made of lymphocyte responses of unresponsive controls and unresponsive patients as measured by our over-all index (TRI). For discussion of the meaning of this figure, see text.

poses of immediate discussion it may be defined as a composite measure utilizing our 6 indices of adrenal cortical activity. We have separated those control subjects who show significant positive values of TRI from those who do not in both the target ball and pursuit meter tests.

On the left side of Fig. 5 a comparison is made of lymphocyte behavior between controls who showed no significant increases in TRI and controls who did show significant TRI changes for both target ball and for pursuit meter tests. It may be seen that the

responsive controls (+ TRI) show declines in lymphocytes except for an insignificant rise in the second post test hour of the pursuit meter test and these declines are significantly different for the immediate post-stress pursuit meter test and the 2-hour post-stress target ball test from the rises in lymphocytes that occur in the controls whose adrenal cortices are nonresponsive in terms of their TRI values. Only the rises in the second of our 2 poststress determinations in the 2 tests are here significantly different from the pretest values but the movement in opposite directions for responsive and nonresponsive *control subjects* is apparent.

On the right of the figure we compare the same nonresponsive controls (above) to non-responsive patients (below) and here we see that in general the patients tend to show small but not statistically significant declines in lymphocytes after the tests in comparison to the elevations of the nonresponsive controls.

We believe that these data make possible an interpretation of all our lymphocyte findings along the following lines. Epinephrine has been demonstrated to produce marked elevation of circulating lymphocytes in animals(25) and in man(26). This is usually followed by a lymphopenia as a result of adrenal cortical activity. Strong stresses as in the case of the heat stress of Fig. 4 excite both the adrenal cortex and medulla but in normal persons the cortical action swamps out the lymphocytosis due to epinephrine and produces a net lymphopenia. Weaker stresses such as those of the target ball and our current pursuit meter stresses (in contrast to our earlier more stressful pursuit meter tests(22)) do not excite the adrenal cortex in our subjects with negative TRI values. Presumably we therefore get a lymphocytosis only, as a result of release of epinephrine. The unresponsive patients in contrast to the unresponsive controls fail even to show an epinephrine effect, an observation consistent with a variety of work indicating autonomic sluggishness in the schizophrenic(27). In Part II we shall further consider epinephrine as a pituitary-adrenal cortical activator.

## DISCUSSION

One might think that the unresponsivity of the schizophrenic patients might be due to lack of interest and general other-worldly detachment from the experimental procedure, but this cannot account for it. In the stresses with heat and cold reported elsewhere both patients and controls were exposed in a room at the same time to the abnormal temperatures and both groups sweated or shivered alike. The normals showed enhanced adrenal activity and the patients did not. Moreover, the purely internal stress of assimilating large amounts of sugar administered in our sugar tolerance tests<sup>5</sup> showed significant differences in responses of the adrenal cortex in patient and control groups. Finally, as will be seen in Part II, a study of responses to the injection of 25 mg. of ACTH in 25 normals shows that all of them respond in all the indices, while only 5 of 25 schizophrenic patients respond in a way at all similar to that of the normal group. As to psychological tests, including performance on the pursuit meter and the target ball tests, the patients were cooperative and their investment of interest in the situation seemed to be as great or greater than that of the control subjects.

Getting up in the morning has long seemed to be a stress to many of us, and we have reported that people in general show an enhanced adrenal cortical output accompanying the start of the day's activities. For example, there is an average rise of  $50 \pm 14\%$  over the sleeping level in the output of 17-ketosteroids during the first 2 hours after rising and this tends to decline progressively during an uneventful day (17, 21, 28).

The daily rhythm of adrenal cortical activity of psychotic patients as a group is significantly less pronounced than that of controls. The ratios of the night rate of 17-ketosteroid excretion divided into the morning rate in a group of 10 women suffering from involutional psychosis was studied before, during, and after a course of electric shock treatments. Most of these women showed good psychiatric progress during and following the weeks of shock therapy. The group

pretreatment output of 17-ketosteroids in the morning was only 3% higher than their night level in contrast to an increase in the first 2 hours after waking in normal persons of 50% over the night level. This value increased in the patients from 3% to 32% during the treatments, and averaged 25% a month after the treatments were over. We thus see that improving treatment tends to normalize the rhythms (29) although in this group it never reached the 50% level for normal persons.

The discussion so far has indicated that a variety of specific work-a-day stresses releases in normal persons adrenal cortical hormones that modify a number of metabolic processes. The schizophrenic is not apparently deficient in over-all adrenal cortical hormone output. It is known that these hormones are released from the cortex in animals at a constant rate in the absence of pituitary. It is the patients' stress responses that are defective and these involve varying hormone output to meet fluctuating demands.

What then do these findings mean in terms of psychosis? They certainly do not mean that adrenal stress response failure is the one and only "cause" of the psychosis though it may well be one of a number of important factors that are involved.

A psychosis is primarily a failure in interpersonal relations determined by a breakdown in higher mental processes which in turn are dependent upon the dynamic patterning and conduction of impulses in the brain. Our work indicates that one of the most conspicuous indices of failure in the patients is in the adrenal regulators of salt balance at the time of stress. The electrolyte, potassium, regulated by the adrenal cortex is a substance of great importance in the excitability of nerve and in the generation and propagation of its action currents. Patterns of nerve messages constitute the physical basis for thought and conduct. The most consistent of our adrenal indices separating patients from controls in stressful situations are our data of potassium excretion. We (30) have shown alterations in the content of potassium in rat brain following stress and the regulation in rats of brain potassium by the adrenal cortex. It is possible that faulty potassium metabolism in the face of

<sup>5</sup> See Freeman and Elmadjian paper elsewhere in this issue.

the repeated stresses of daily life may be an important cumulative factor in the development of a psychosis.

It may be that endocrine deficiencies of the sort we have been discussing and which may perhaps be genetically determined make some persons more vulnerable to the stresses of living than others. Such persons may never become psychotic if their lives present few problems, but under more severe environmental and personalized stresses their endocrine defects may result in brain malfunction with consequent psychotic disturbances.

The schizophrenic patients used in this study have been chronic state hospital cases 20-40 years old and with an average duration of hospitalization of  $2\frac{1}{2}$  years. The adrenal cortical responses of these patients may be

different from those of acute early cases. This is especially suggested by experiments reported by Dr. E. F. Gildea at a round table conference at the Montreal meetings of the American Psychiatric Association. He exposed early schizophrenic patients to heat stress and found a uniform lymphocytopenia similar to that of controls and sharply in contrast to our data shown in Fig. 4. Thus, despite the fact that the lymphocyte response is a complex stress index, there may be a fundamental difference in early and in chronic populations of schizophrenic patients.

In the second part of this communication, publication of which will follow, we shall consider the locus of the adrenal stress response failure in psychotic patients and further discuss the significance of the findings.

(References follow Part II.)



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ADRENAL CORTICAL RESPONSES TO STRESS IN NORMAL MEN  
AND IN THOSE WITH PERSONALITY DISORDERS<sup>1</sup>

PART II. ANALYSIS OF THE PITUITARY-ADRENAL MECHANISM IN MAN

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The demonstration that the normal adreno-cortical responsivity to stress fails in schizo-phrenic men generally gives no indication of what part or parts of the pituitary-adrenal mechanism may be the source of the stress-response failure. As indicated in Fig. 6, the pursuit meter and target ball stresses described in Part I of this paper presumably operate on this mechanism through the central nervous system, stimulating the release of pituitary ACTH, which in turn acti-

should effect a "short-circuiting" of the balance of the mechanism. If the schizo-phrenic receiving ACE exhibits adequate responses in our 6 indices then we may con-clude that his end organs and metabolizing tissues are capable of normal response to adrenal cortex hormone. Similarly, if ACTH administration to schizophrenics induces nor-mal responses in our indices the deduction

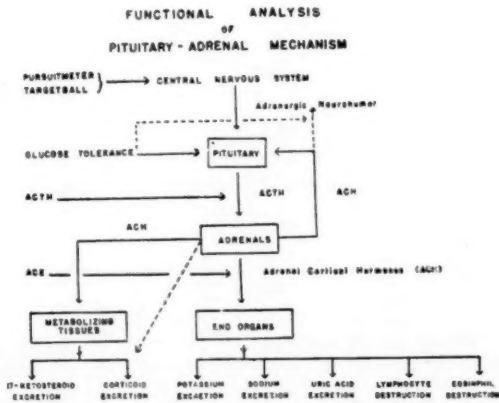


FIG. 6.—The rôle of various experimental procedures in the analysis of the pituitary-adrenal mechanism.

vates adrenocortical secretion. Our measurements involve the effects of this adreno-cortical secretion on end organs or of metab-olizing tissues on the secretory products. Obviously failure of significant change in these measures generally may inhere in faulty functioning of any one (or several) of the components of this system.

In order to effect an analysis of the sys-tem, we have employed the tests indicated at the left of the diagram. The administra-tion of potent adrenal cortex extract (ACE)

<sup>1</sup> Read at the 105th annual meeting of The Ameri-can Psychiatric Association, Montreal, Quebec, May 23-27, 1949.

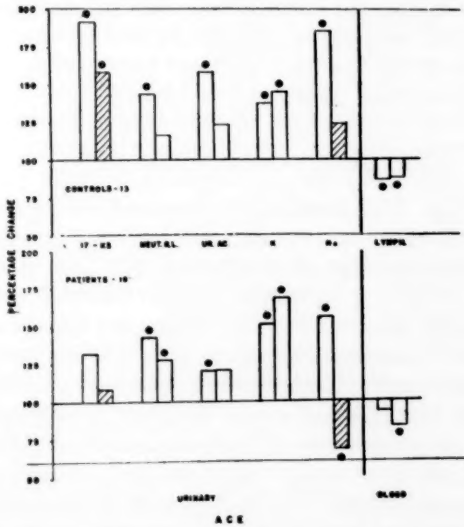


FIG. 7.—The effect of administering lipo-adrenal extract upon the percentage change of various indices of adrenocortical function in control and schizophrenic subjects. Symbols as in Figs. 2 and 3.

is that the schizophrenic's adrenal cortex is capable of response to the normal activat-ing hormone. The adrenocortical response to sugar is mediated by the pituitary(31), and we have employed the glucose tolerance test as a probable means of "short-circuit-ing" the central nervous system.

THE ADMINISTRATION OF ACE

In Fig. 7 we present the mean data of our indices for a group of 18 schizophrenic men and a control group of 13 men each of whom

received 10 cc. of a potent adrenal cortex extract (Upjohn's lipo-adrenal extract). It is at once obvious that these data offer a marked contrast to those of Figs. 2 and 3. First of all, the patient group exhibits increases in all the urinary indices instead of the decrease exhibited by the data of Figs. 2 and 3. Secondly, these increases are statistically significant during either the stress or poststress periods (or in both in the case of neutral reducing lipid and potassium excretion), save for the 17-ketosteroid output data. Thirdly, there is no significant difference in the output data between the control and patient group save in the poststress 17-ketosteroid and sodium outputs, nor do the observed lymphocytopenias differ significantly. We may conclude that generally the end organ responsivity and metabolizing tissues respond to adrenocortical steroid in practically normal fashion in the schizophrenic men tested.

#### THE ADMINISTRATION OF ACTH

Fig. 8 demonstrates the changes in the mean data for our various indices after the administration of a standard 25 mgm. dose of ACTH per subject. This material was standardized by us in terms of biological activity corresponding to an electrophoretically purified preparation made by White and Hadidian (cf. 23). This test was given to 25 control and 25 schizophrenic men. Indications of some responsivity in schizophrenic subjects are had from the significant poststress increases of neutral reducing lipid and uric acid and in the significant rise in stress and poststress potassium outputs. Insignificant changes occur, however, in the urinary 17-ketosteroid and sodium concentrations and in the blood lymphocytes. In contrast every index exhibits significant change in the control group and every urinary index, save the neutral reducing lipid output, differs significantly from the patient data. We are, therefore, led to conclude that the adrenal cortex of schizophrenic men is much less responsive than that of normal men.

This differentiation between normal and schizophrenic men in ACTH responsivity contrasts notably with the situation in psy-

choneurotic subjects. As previously reported (23), data for various measures of adrenocortical response to ACTH are essentially normal in psychoneurotic subjects. This is

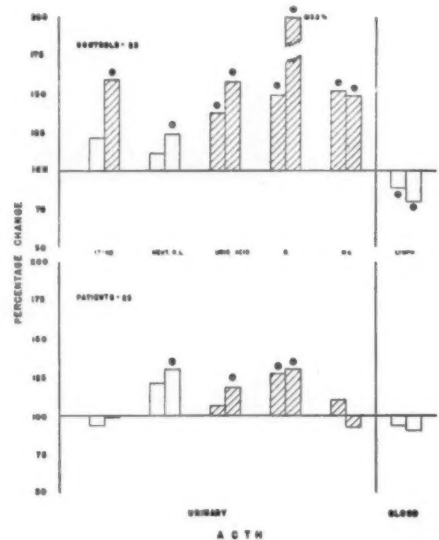


FIG. 8.—Adrenocorticotrophic (ACTH) hormone administration and the changes in indices of adrenocortical function. Symbols as in Fig. 2 and 3.

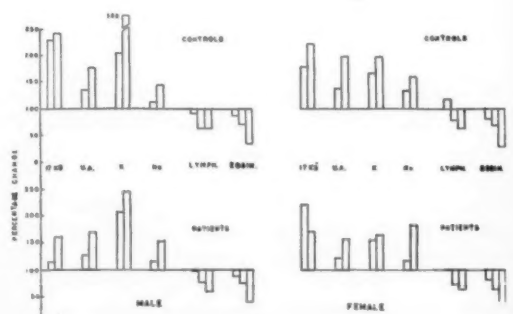


FIG. 9.—Indices of adrenocortical response to ACTH in 12 control male subjects and 11 control female subjects (upper rectangles) compared with the responses of 11 psychoneurotic men and 13 psychoneurotic women (lower rectangles). There is no significant difference of response between the normal and psychoneurotic subjects.

illustrated in Fig. 9, in which are plotted the mean data for groups of 11 to 13 psychoneurotic men and women along with similar data for the same numbers of control subjects. In no single measure is there significant differentiation.

THE TOTAL RESPONSE INDEX (TRI)

The foregoing analysis indicates that the locus of the defective response to stress of schizophrenics lies in the adrenal cortex. The data presented are, of course, mean values for the groups of subjects tested. The indications of a small degree of responsivity to ACTH in the schizophrenics' data (Fig. 8) suggest that certain of these subjects may be fairly responsive whereas others may not be. In order to assess individual responsivity we have constructed a total response index (TRI) that combines our various

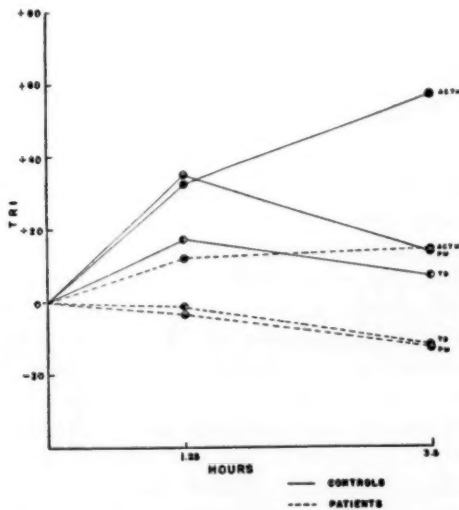


FIG. 10.—Variations in the stress and poststress values of the total response index (TRI) in the target ball (TB), pursuit meter (PM) and ACTH tests. Solid lines, mean data for controls; dotted lines, mean data for schizophrenics.

measures in a single measure. The TRI is equal to the sum of the stress and poststress percentages increases in the urinary measures plus twice the percentage decrease in blood lymphocytes divided by the number of observations. A TRI value greater than 0 indicates a degree of positive response, a negative TRI indicates a greater or lesser failure of response. We may, of course calculate a TRI value for the stress and poststress periods separately, and in Fig. 10 this is illustrated for 3 of our tests. The mean stress (1.25 hour) and poststress (3.5 hour) values for the control (solid lines) and schizophrenic men (dotted lines) demonstrate: (a) a typical stress rise and post-

stress fall in both the target ball and pursuit meter tests for the control subjects contrasting with a decline below the prestress level for the schizophrenic men; (b) a greater quantitative response to the pursuit meter stress in the normal subjects in contrast to identical curves of unresponsivity for the 2 tests in the schizophrenic men; (c) a typical rising curve of response to ACTH for the control subjects contrasting with a quantitatively lower curve for the schizophrenic subjects.

We have previously(23) indicated that a TRI value of +20 or greater may be taken as an indication of a positive adrenocortical response. In Table 2 we present the data on the frequency of occurrences of such values in both groups of subjects in the various tests. It will be seen that every one of our 25 control subjects had a TRI of +20 or greater in the ACTH test, whereas only 7 (or 28%) of the schizophrenic men were positive responders. If we assume that end-organ and metabolizing tissue responsivity are identical in the 2 groups (*vide* Fig. 7) then it follows that 72% of our schizophrenic subjects had unreactive adrenal cortices. In the pursuit meter test, 47.8% of the normal subjects exhibited a TRI value of +20 or greater. We take this to indicate that the test was a clearly significant stress to approximately one-half of the control subjects. Among the schizophrenic men, only 15.8% of the men were positive responders on this basis. If we assume that the ACTH data indicate that 28% have adequately responsive adrenal cortices, then the presence of a similar proportion of responders to the stress test would suggest that the presence or absence of an adequately responding adrenal cortex is the limiting factor to the exhibition of responsivity; actually we would expect, on this basis, 13.4% positive responders and observe 15.8%. Similarly for both the target ball and glucose tolerance data the proportion of positive responders in the schizophrenic groups is close to 28% of the percentage of positive responders observed in the corresponding control groups. Again, evidence of an adrenocortical locus of the stress response failure in schizophrenic men is had.

The fact that 100% of our normal sub-



jects gave TRI values of +20 or greater after the administration of 25 mgm. of ACTH indicates merely that this dosage is sufficient to evoke significant adrenocortical secretion. The 72% of schizophrenics failing to exhibit such responsivity may be capable of full adrenocortical secretion but require simply larger amounts of ACTH for its evocation; in short, an adrenal cortex threshold may be involved. Accordingly, we selected 8 schizophrenic men having TRI values of less than +20 after 25 mgm. of ACTH were administered and injected them with 75 mgm. dosages. In Fig. 11 we pre-

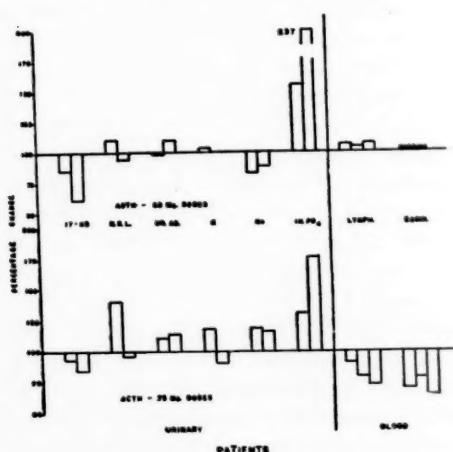


FIG. 11.—Mean changes in various urine and blood functions in 8 schizophrenic men classified as nonresponders to a 25 mgm. dose of ACTH (upper rectangles) and their responsivity to a 75 mgm. dose (lower rectangles). Lymphocyte and eosinophile responsivity at the 75 mgm. dose level are statistically significant.

sent the mean values of various urinary and blood indices in this group at these 2 dosage levels. Although there are indications of increased response to the higher dosage in the various urinary measures a statistically significant difference from the lower dosage values is not attained. The clear lymphocytopenia following the 75 mgm. dosage is, however, quite significant, and it should be noted that a significant eosinopenia also occurs. The evocation of the lymphocyte and eosinophile responses suggests that the nonresponder either differs only quantitatively at the adrenocortical level from the responder or that lymphocytopenic hormones are evokable by ACTH whereas

other types (*e. g.*, those concerned with increasing electrolyte excretion) are not. The fact that a significant lymphocytopenia is measured in the data for schizophrenic men following pursuit meter and target ball stress (Figs. 2 and 3) suggests a greater lability of this system in at least a proportion of the schizophrenic subjects. Whether or not the appearance of a significant lymphocytopenia with sufficient ACTH dosage signifies a quantitative or a qualitative difference in adrenocortical secretion or threshold, the indications of abnormal responsivity remain.

#### ADRENOCORTICAL RESPONSIVITY AND NUTRITION

We have asked ourselves what may be the basis of this abnormal adrenocortical responsivity. One consideration is that the nutritive state of the patient may severely limit the supply to the adrenal cortex of substances essential to increased secretory activity. It has been demonstrated, for example, that adrenal ascorbic acid is depleted in the course of secretory activation (5, 6). An inadequate intake of this vitamin might therefore be responsible for inadequate responsivity. Other nutritional factors (*e. g.*, pyridoxine) may similarly be involved. To test the probability that the hospital dietary might act to limit adrenocortical responsivity we selected 9 schizophrenic men and fed them over a 12- to 14-day period a high-protein, high-vitamin supplement to the regular hospital diet. The details of this nutritional study are published elsewhere (32). Summarizing them briefly, we found that after a weight loss occurring after one day of the régime all the subjects (save one who was overweight) gained weight, and the average rate of weight increase was 0.2 lb. per day (Fig. 12). Each subject (save one) at the conclusion of the dietary régime exhibited a greater or lesser decline in hemoglobin concentration (Fig. 13), and each subject without exception had a clear rise in plasma ascorbic acid levels (Fig. 13). Finally, measurements of plasma protein concentrations at the initiation and conclusion of the régime disclosed changes in total protein, albumin and globulin (Fig. 14) characteristic of nutritional repletion (33) and similar to plasma protein changes

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occurring on remission after electroshock therapy(34). Among these 9 schizophrenic men were two "responders" (TRI of +20 or greater) and 7 nonresponders. It should

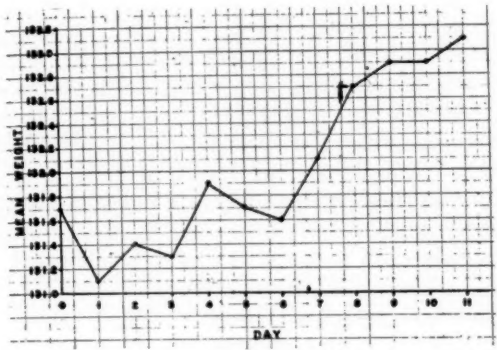


FIG. 12.—Mean weight changes in a group of 9 schizophrenic men receiving a high-protein, high-vitamin dietary supplement.

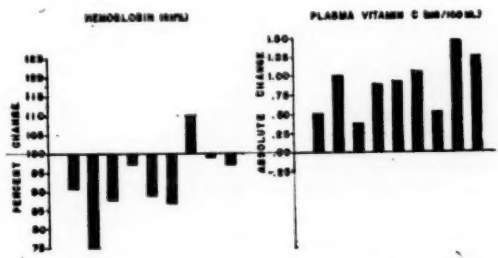


Fig. 13.—Percent changes in blood hemoglobin (left) and absolute increases in plasma ascorbic acid (right) in the 9 subjects on the dietary supplement.

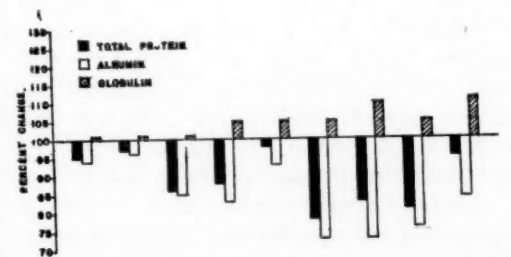


FIG. 14.—Percent changes in plasma total protein, albumin, and globulin in the 9 subjects on the dietary supplement.

be noted that the responders' weight, blood hemoglobin, plasma ascorbic acid, and plasma protein changes were entirely similar to those seen in the nonresponders.

At the conclusion of the dietary supple-

ment régime each subject received an injection of our standard dose of 25 mgm. ACTH. In Fig. 15, we plot the mean pre- and postsupplement percentage change values (stress and poststress combined) of our urinary and blood indices as well as the mean TRI for the 2 types of subject. It may be seen that the 2 responsive men exhibited the same sort of responsivity before and after the supplement régime, whereas the nonresponders showed no notable change in responsivity, the slight net increase being in no sense statistically significant. Actually, the data for one of the 7 nonresponders

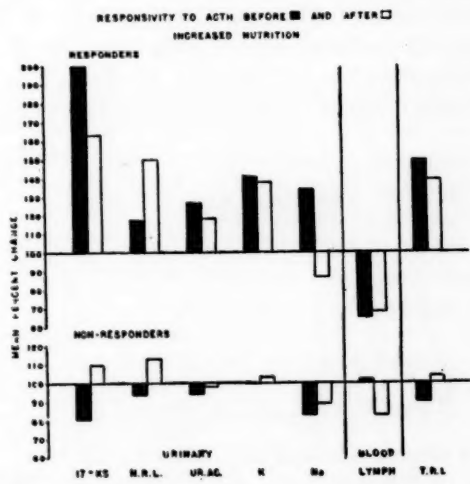


FIG. 15.—Responsivity of 2 schizophrenic responders (upper rectangles) and 7 nonresponders to the standard 25 mgm. dose of ACTH before and after receiving the dietary supplement.

gave a TRI of over 20, so the possibility of an occasional restoration of responsivity is suggested.

### DISCUSSION

The uncovering of impaired adrenocortical responsivity to ACTH in a majority of the schizophrenic subjects impels consideration of the presumable bases not only of this relative unreactivity but also of the implications of the presence of a distinct proportion of reactive schizophrenic subjects in this and each of our stress tests.

We have excluded a frank Addisonianism in these unreactive subjects, and we have demonstrated that a nutritive depletion cannot offer a satisfactory explanation. Two

major possibilities appear to offer themselves: (a) these subjects are in an equivalent of the stage of exhaustion of the adaptation syndrome or (b) the secretions of their adrenal cortices differ qualitatively from those of normal men. The former suggests a quantitative limitation to adrenocortical secretion; these men are secreting maximally in the basal state and are incapable of further hormone production—they have little or no secretory reserve. The evocation of a clear lymphocytopenia in unreactive men with the high dosage of ACTH tends to contradict this notion. Again, as far as the lymphocyte response is concerned, Parsons, Gildea, *et al.* (26) have demonstrated in a group of psychotic men a clear lymphocytopenia following electroshock, as though an extremely intense stress may break through

the data on neutral reducing lipid response scarcely differentiates normals from schizophrenics, and this is especially notable in the ACTH test (Fig. 8), whereas 17-ketosteroid output changes invariably differentiates the 2 groups. It almost appears as if the schizophrenic men's adrenal cortices fail to secrete significant amounts of 17-ketosteroid precursors in response to stress, but do secrete neutral reducing lipid precursors and that the latter may be substances acting particularly on the lymphatic system. We hope to resolve this possibility in future studies of the exact chemistry of adrenocortical substances in schizophrenic men.

Let us consider now the schizophrenic subjects exhibiting significant adrenocortical responsivity. The total of such subjects is

TABLE 2  
THE TOTAL RESPONSE INDEX OF VARIOUS SUBJECTS IN THE STRESS TESTS

Test	Subjects	Mean TRI	% of subjects with score of 20 or greater	Ratio of normal responders to schizophrenic responders
ACTH	Normal (25)	46.2	100.0	
"	Schizophrenic (25)	12.0	28.0	3.6
Pursuit meter	Normal (46)	22.1	47.8	
"	Schizophrenic (36)	-2.7	15.8	3.0
Target ball	Normal (36)	11.5	32.5	
"	Schizophrenic (20)	-6.7	10.0	3.3
Glucose tolerance	Normal (47)	22.1	48.6	
"	Schizophrenic (38)	5.7	15.0	3.2

and evoke a secretory reserve. The notion of a qualitative alteration in adrenocortical secretion in the unreactive men receives support from the evocation of a significant lymphocytopenia in certain tests, unaccompanied by comparable response in other indices. Thus the ratios of mean stress percentage change in lymphocytes to the mean uric acid percentage change are 1:1.2 and 1:1.4 for the normal subjects in the target ball and pursuit meter tests, respectively; the corresponding ratios for the schizophrenics' data are 1:1.0 and 1:1.05. In the ACTH test these ratios again are 1:1.8 for the control subjects and 1:1.1 for the schizophrenic men. It is as if the schizophrenic men secrete lymphocytopenogenic substance more readily than they do uric-acid-releasing substance. An even greater disparity exists between the lymphocytopenic and electrolyte responses in the schizophrenic men. Again,

not large, but as reported above (Table 2) a little less than 1 schizophrenic in 3 gives indication of positive adrenocortical response to either ACTH or of a response comparable to normal in our 3 principal stress tests (pursuit meter, target ball, glucose tolerance). On the basis of our analysis of the pituitary-adrenal mechanism (Fig. 7) the positive responders to the pursuit meter and target ball tests presumably have had activation of every step in this mechanism. Taking the data for the 14 schizophrenic men having TRI values of 20 or greater in the 3 stress tests, we have compared them with the data for the same number of normal subjects having a similar distribution of TRI values.

Since the percentage change in neutral reducing lipid excretion does not, by and large, distinguish normal from schizophrenic subjects we have taken the mean stress and poststress change in this variable and divided



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it into the corresponding mean percentage change of our other stress indices. The derived data are presented in Table 3. It is clear that this ratio is quite different in the 2 groups. Thus for the normal subjects it varies from 1.30 to 1.38 for the urinary indices, whereas among the schizophrenics' data the range is 0.80 to 1.12. Furthermore, for all indices the value for the schizophrenic subjects is less than for the normals. This suggests at once a different pattern of stress response even in those schizophrenic subjects who are adrenocortically responsive to stress. The indication is that in terms of neutral reducing lipid production there is first of all relatively less response in the other indices

TABLE 3

THE RATIO OF MEAN PERCENTAGE CHANGE IN NEUTRAL REDUCING LIPID OUTPUT TO THE MEAN PERCENTAGE CHANGE IN OTHER INDICES

The data are those of the 14 schizophrenic men classified as positive responders to the 3 stress tests and a similar group of normal subjects (see text).

Response index	Ratio	
	Schizophrenic men	Normal men
17-ketosteroid output . . . . .	1.12	1.35
Uric acid output . . . . .	0.80	1.38
Potassium output . . . . .	0.87	1.31
Sodium output . . . . .	0.94	1.30
Lymphocyte number . . . . .	0.61	0.82

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and secondly a differential response. Thus uric acid and potassium excretion changes are least in the patients, sodium output intermediate, and 17-ketosteroid output largest but not up to the normal level. These data again are consistent with the notion that schizophrenic men secrete corticosteroids differently in response to stress, pointing again to a "block" in the adrenal cortex.

The foregoing analysis does not exclude completely the possibility of abnormal function in schizophrenic men of either the central nervous or pituitary components of the pituitary-adrenal stress mechanism. The slightly higher proportion of schizophrenic responders in the ACTH test suggests this, but a much larger statistical array would be required to establish such cases. Parsons, Gildea, *et al.* (26) used insulin shock, electro-

shock, and epinephrine injections as 3 different physiological stresses in psychotic patients. They found epinephrine to produce an immediate and marked increase in lymphocytes followed by a fall that is maximal in the third hour in 6 normal controls, and similar curves were obtained for 8 psychotic patients (schizophrenics and manic-depressives). From this they conclude that failures to respond to psychological stress (in which they confirm us) must be mediated by failure of the central nervous system to excite the pituitary since both groups responded similarly to the epinephrine. We do not believe this conclusion justified for the following reasons. (a) Quite apart from any stimulation of epinephrine on the pituitary this substance directly in itself releases lymphocytes and such a marked release is followed by a *compensatory depression*. Elmadjian *et al.* (35) have found this type of compensatory lymphocytopenia in adrenalectomized rats following epinephrine injection. (b) Epinephrine markedly increases blood sugar to an extent comparable to our sugar tolerance values and we have shown that sugar is a stress causing lymphocytopenia (23). We also find that 1 patient in 3 responds as do normals to sugar stress. For these 2 reasons we would not expect to find significant differences in lymphocyte responses to epinephrine between a small group of patients as compared with controls.

The shock treatments are very drastic stresses. We have found that large doses of ACTH (75 to 100 mg.) will excite adrenal responses in schizophrenic patients who fail to respond to the 25 mg. doses that strongly excite responses in normal persons. We therefore would expect that insulin therapy and electroshock therapy would produce responses in patients, and indeed we have found that such responses do occur (unpublished data).

Finally, our data show that the lymphocyte response is by no means as good a measure of adrenal activation as are some of our other indices, especially urinary potassium changes. It should be emphasized that the crucial test for adrenal cortical activation *per se* is the response to ACTH, and this we find to be defective in 72% of the patients as compared to our controls.

## SUMMARY

1. Six indices of adrenal cortical activation have been compared in groups of normal male subjects and schizophrenic male patients when they were subjected to a variety of stresses. The indices are changes in output of urinary sodium, potassium, uric acid, 17-ketosteroids and neutral reducing lipids together with changes in the number of circulating lymphocytes. The stresses have been the target ball frustration test, operation of a pursuit meter (each test lasting one hour), the effects on our indices of adrenal cortical extract and of pituitary adrenocorticotrophin.

2. Responses of our 6 adrenal cortical indices and also eosinophile responses to injected adrenocorticotrophin were determined for groups of male and female psychoneurotic patients and compared to normal controls.

3. The tests all involved significant numbers of patients and controls and the results have been treated statistically.

4. Our data indicate a highly significant failure of normal adrenal stress responses in the schizophrenic population as compared with the control population.

5. The failure occurs principally at the level of the ability of the adrenal cortex to respond to adrenocorticotrophin.

6. This failure was not corrected by a dietary supplement rich in proteins and vitamins.

7. These findings are discussed in relation to the etiology of schizophrenia.

8. Psychoneurotic patients in contrast to schizophrenics respond in a normal fashion to injected adrenocorticotrophin.

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# CARBOHYDRATE AND LYMPHOID STUDIES IN SCHIZOPHRENIA<sup>1</sup>

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This paper deals with a series of investigations concerning certain phases of carbohydrate metabolism in schizophrenic patients and the endocrine mechanisms that might serve as a background for the abnormalities uncovered in these researches. The utilization of glucose not only has been studied as a physiological characteristic by itself but has also been employed as a technique in promoting a particular type of endocrine stimulation involving the adrenal cortex. The relationship of the adrenal cortex to sugar metabolism has been amply demonstrated by various investigators(1, 2). The index of adrenocortical reactivity which we have used has been the decrease in the level of the absolute lymphocyte count. Lymphopenia has been shown to follow adrenal stimulation whether owing to administration of an anterior pituitary extract(3) or to exposure of the individual to trying situations(4). From this point of view, the ingestion of glucose has been used as a stressful procedure.

Abnormalities in sugar tolerance in psychoses have been noted by many investigators(5) but, in general, the results have been left at a descriptive level. Our experience has been primarily with the Exton-Rose technique(6) because of the shorter duration of the test procedure and the greater simplicity of the interpretation. In this method, under fasting conditions, two doses of 50 grams of glucose are administered 30 minutes apart. Blood samples are obtained just before each dose of glucose is ingested and 30 minutes after the second dose. Thus, the test lasts one hour and includes the measurement of 3 blood sugar values.

The characteristic values for normal and psychotic subjects are shown in Fig. 1. The mean trends for 20 normal males (age 20 to 40) show a sharp upward trend after the first dose of glucose but a slight decline

after the second. In the patients (age 20 to 40) there is a similar rise for the first 30 minutes and a subsequent rise after the second dose of glucose. It is the behavior of the blood sugar in the second half hour that differentiates patients as a group from normal subjects as a whole. Since not all individuals conform to the mean trends, the subjects were divided into 2 groups: those showing a downward trend in blood sugar

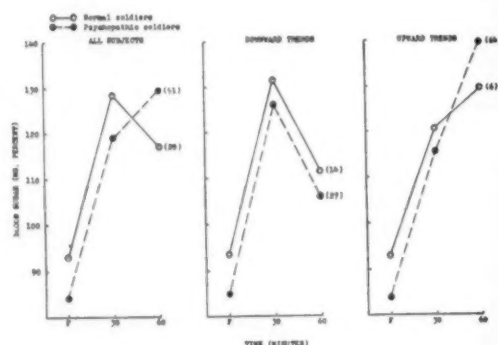


FIG. 1.— Means of Exton-Rose glucose tolerance tests on normal and mentally disturbed soldiers.

TABLE 1  
MEAN VALUES OF EXTON-ROSE GLUCOSE TOLERANCE TEST BY DIAGNOSTIC GROUPS

Diagnosis	No.	Blood sugar		
		Fasting, mg.	30 min., mg.	60 min., mg.
All psychoses . . . . .	66	84	117	130
Schizophrenia . . . . .	38	82	119	127
Other psychoses . . . . .	28	85	116	134
All nonpsychoses . . . . .	25	84	122	129
Normal controls . . . . .	20	93	128	117

after the second dose of glucose and those showing an upward trend. Approximately two-thirds of the normal subjects and one-third of the patients are in the former category, while one-third of the normal controls and two-thirds of the patients show the upward trend, *i. e.*, reduction in glucose tolerance. Thus the differentiation is not wholly complete. This type of response is not confined to schizophrenic subjects, since it is present in equal degree in other types of psychoses and also in nonpsychotic individuals with mental disturbances (Table 1).

<sup>1</sup> Read at the 105th annual meeting of The American Psychiatric Association, Montreal, Quebec, May 23-27, 1949.

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It is a phenomenon, therefore, widespread throughout all phases of mental disease. The subjects described in the previous figures were all in an acute phase of their mental disorder, the average duration of illness being 6 months. It should be noted, however, that similar findings are obtained in schizophrenic patients confined to a hospital for many years (7).

The consistency of the results was, of course, an immediate problem. We have investigated the sugar tolerance of 10 chronically ill schizophrenic patients over a period of 5 weeks, performing the test pro-

cedure did not change in any appreciable degree in this interval of time.

The influence of psychological factors on the sugar tolerance is worthy of mention. Since the reduction in tolerance is not specific to schizophrenia it follows that it is indicative of a fundamental trend in mental disturbance. Our hypothesis is that it is due to "tension" since (1) there is some inter-relationship with emotional disturbances as shown by the Rorschach test; (2) there is in some cases a "normalization" of the sugar tolerance with diminution of the psychotic behavior; (3) a normal glucose tolerance

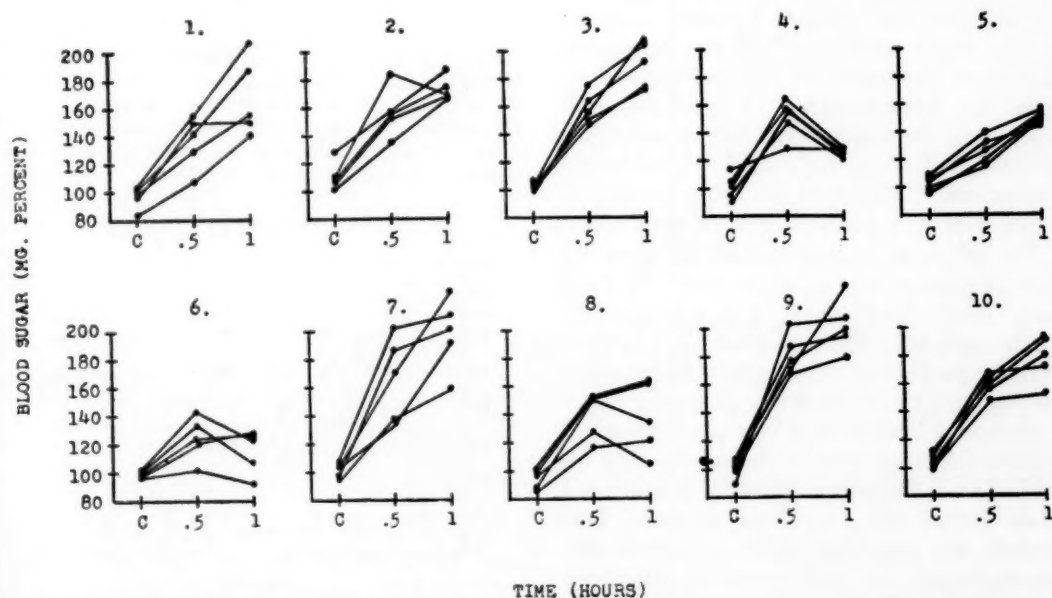


FIG. 2.—Five glucose tolerance tests performed at weekly intervals on 10 schizophrenic patients.

cedure at weekly intervals. The results are shown in Fig. 2. There are 3 patients whose sugar tolerances tend to be of the normal type (numbers 4, 6, and 8). The other subjects have diabetic-like trends. Within the individual subject, the consistency of the trend is high, there being only an occasional exception, although there is some variation in the absolute values. It should be mentioned that apprehension of the test procedure apparently had little influence in the establishment of the specific blood sugar levels since there was no consistent diminution in the values during the course of the study. It should also be noted at this time that the psychiatric status of the patients

can be changed to an abnormal (reduced) tolerance by the administration of a stress procedure.

So far as the first factor is concerned, Rorschach tests (8) in psychotic subjects show that those who exhibit abnormal tolerances (approximately two-thirds in number) are in general more reactive and less constricted, *i. e.*, not capable of as much control as the group with the normal trends. Such results would be consistent with the hypothesis that such individuals are either under more "tension" than the other types of subjects or are unable to control their emotional expression as much as the latter.

The relationship of the sugar tolerance

to the psychiatric status of the patient is still a moot point. Diethelm(9) found marked variations in the blood sugar values corresponding with the mood of the patient. Proctor, Dewan, and McNeel(10) using insulin shock therapy noted a lessening of abnormal trends in sugar values in those patients who showed marked improvement. Freeman and Zabarenko(11) studied 29 patients treated with electroshock therapy and measured sugar tolerances at intervals before and after their treatment was completed. In individual instances where there had been apparently a marked solution of the emotional problems there seemed to be a corresponding change (toward normal) in the sugar tolerance. Where a marked degree of emotional tension still existed despite the disappearance of the psychotic symptoms, the sugar tolerance remained abnormal. When the psychiatric status of the patient was unchanged by the therapy, the sugar tolerance showed little or no change.

The effect of a stress procedure upon the type of glucose tolerance was noted by Freeman, Rodnick, Shakow, and Lebeaux(8). Their subjects, both normal and schizophrenic, performed on a pursuit meter under fasting conditions for one hour during which a glucose tolerance test was performed. A control tolerance was measured the day before or after the pursuit meter was employed. They found that, in those subjects, both normal and psychotic, with a normal glucose tolerance, the employment of the stressful procedure resulted in an alteration of the glucose tolerance in the direction of an upward trend in the one-hour reading similar to that characteristically found in the patients (Fig. 3). In subjects with a previous abnormal tolerance the values were not significantly affected, possibly because the degree of emotional tension already present was sufficient to block the introduction of new stress factors.

The activation of the adreno-cortical secretions by stressful procedures was demonstrated in man by Pincus and Hoagland(12). It was also found that the fall in the blood lymphocytes under psychomotor(13) or heat stress(14) was distinctly less marked in schizophrenic subjects than in normal controls. Accordingly, to determine whether the

abnormal glucose tolerance found in patients was influenced by the degree of adrenal cortical activity, simultaneous studies of the

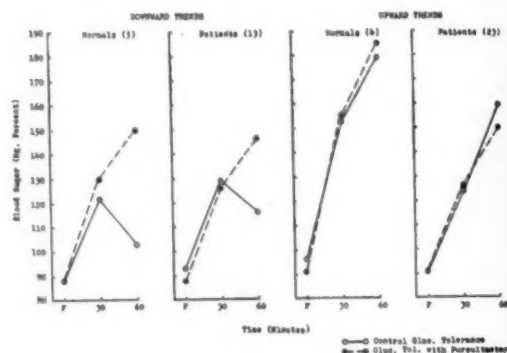


FIG. 3.—Mean values for glucose tolerances obtained (1) under basal conditions; and (2) during the operation of a pursuit meter in normal and schizophrenic subjects, divided on the basis of downward or upward trends in the blood sugar in the second half-hour of the control test.

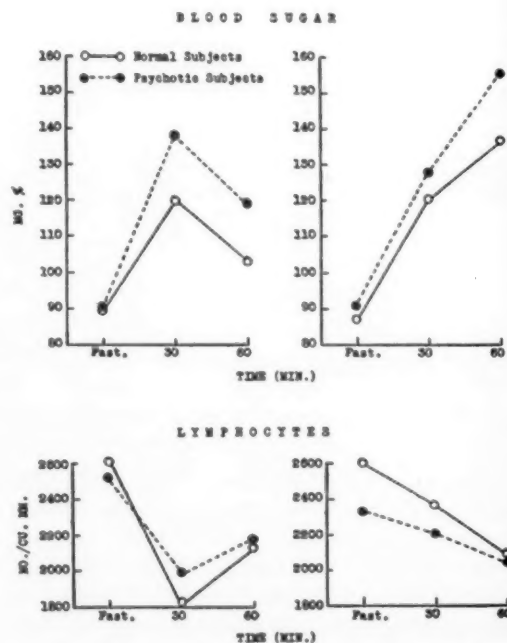


FIG. 4.—Means of blood sugar and lymphocyte values in normal and schizophrenic subjects undergoing Extton-Rose glucose tolerance tests, divided into those showing downward and upward trends in the blood sugar levels in the second half-hour.

blood lymphocytes were carried on in 21 normal subjects and 35 schizophrenic patients subjected to the Extton-Rose glucose tolerance test. In Fig. 4 are seen the mean

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values for the 2 types of subjects when they are divided into 2 groups on the basis of whether the glucose trend is normal or abnormal. The lymphocyte values move in an opposite direction to that of the blood sugar levels. The patients as a group show lesser changes in the lymphocyte values than the normal subjects despite the fact that their blood sugar levels are higher. Further analysis of the data showed that despite the apparent converse trends in the first half-hour the influence of the blood sugar level on the lymphocyte values was not accurately evident until after the second dose of glucose had been ingested, apparently owing to a time lag in activity. There was no significant correlation between the changes in blood

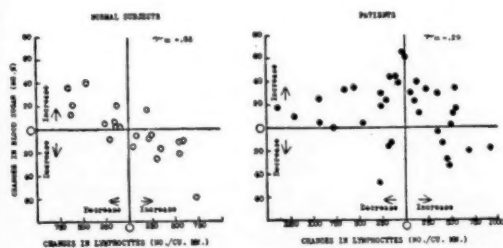


FIG. 5.—Scatter diagrams illustrating relationship between changes in blood sugar and changes in lymphocytes in second half-hour of Exton-Rose glucose tolerance test in normal and schizophrenic subjects.

sugar levels with those of the lymphocyte values until the second half-hour of the test. At this time, however (Fig. 5), in the normal subjects there is a high inverse correlation ( $r = -.85$ ) between the changes in the blood sugar and the changes in the lymphocytes. In the patients, the relationship is much poorer ( $r = -.29$ ). Not only is the scatter wider in the left upper and right lower quadrants but there are also 15 patients (43%) whose values lie in the other quadrants where the relationship is positive. Thus, we may conclude that in almost half the patients the administration of glucose does not have an effect upon the lymphoid processes as it does in normal individuals.

A review of the historical data on these patients indicates 2 findings: (1) the patients with the inverse or "normal" relation-

ship tend to show more indications of retained affectivity and have a more fluid type of symptomatology than do the patients with the positive or "abnormal" relationship; (2) the former group have had a shorter period of hospitalization (median value, 9 months) in contrast to the latter group where the median is 5.3 years. In short, there seems to be some relationship between the normality of the lymphocyte-glucose relation-

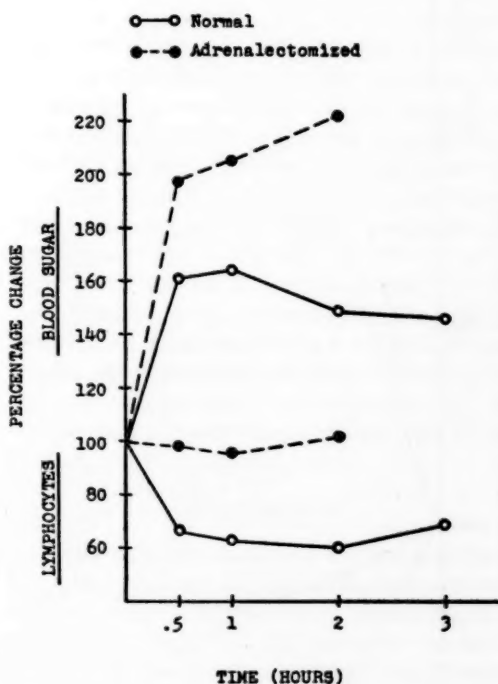


FIG. 6.—Mean percentage changes in blood sugar and lymphocytes following the administration of glucose to normal and adrenalectomized rats.

ship and the relative acuteness and lack of rigidity of the psychotic manifestations.

In order to determine whether the relative failure of the lymphocytes to correlate with the blood sugar trend observed in half the patients is due to adrenal deficiency, animal experimentation has been utilized. Twelve normal and 11 salt-fed adrenalectomized rats (15) were given a 2-dose glucose tolerance test, the dextrose being administered in amounts comparable to their weight (1 cc. of a 50% glucose solution at 30-minute intervals). The results are shown in Fig. 6 in mean percentage changes from

the control values. In the normal rats, the increase in blood sugar in the first hour is accompanied by a sharp fall in the lymphocyte counts. As the blood sugar falls, the lymphocyte count tends to increase. In the adrenalectomized rats, an increase in blood sugar that is more marked than in the normal rats is accompanied by no significant variation in the lymphocytes. It is there-

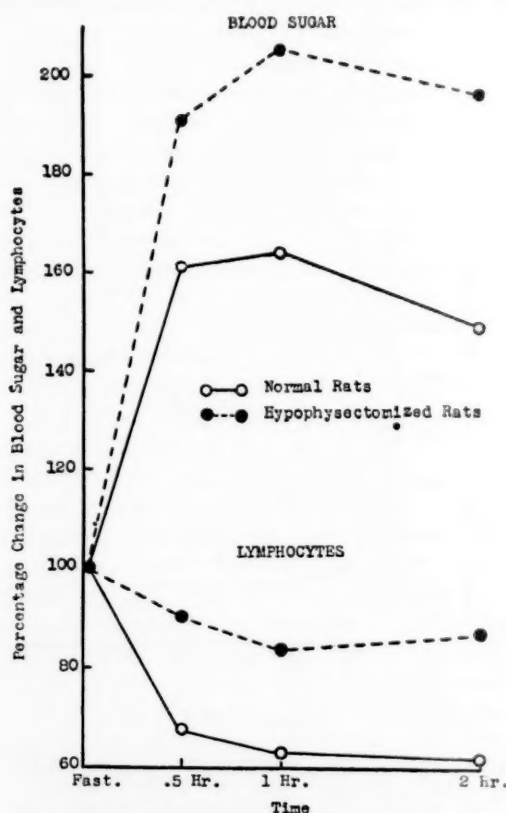


FIG. 7.—Mean percentage changes in blood sugar and lymphocyte values of normal (12) and hypophysectomized (43) rats during a 2-dose glucose tolerance test.

fore evident that the functioning of the adrenal glands is essential for the lymphopenic response following the administration of glucose.

The anterior pituitary is an essential factor, however, in this response, as shown in Fig. 7. The mean lymphopenic response to glucose (in percentage change) of 12 normal rats is compared with that of 43 hypophysectomized rats (16). It is evident that, despite the greater elevation of blood sugar

in the hypophysectomized rats, the fall in the lymphocyte count is definitely less than that of the intact animals. It seems probable, then, that the adreno-cortical stimulation by glucose is mediated through the anterior pituitary.

Despite the abnormal sugar tolerances of the patients, the production of insulin is not an important factor in this relationship, as shown by Fig. 8. Rats were rendered diabetic by the administration (16) of alloxan

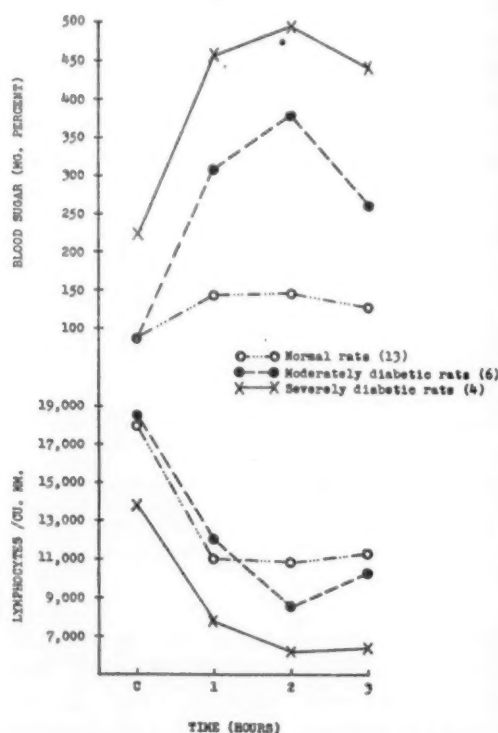


FIG. 8.—Means of blood sugar and lymphocyte values of normal and alloxan-injected rats during the course of a 2-dose sugar tolerance test.

(40 mg./kg. body wt. i.v.), and their lymphocyte responses to glucose were compared with those of normal rats. Six of the alloxan-injected rats presented a picture of mild to moderate diabetes. Their fasting blood sugars were normal and the increase in blood sugar after the ingestion of glucose was moderately high. Their lymphopenic response was on the whole similar to that of the normal rats. Four alloxan-injected rats showed a reduction in tolerance similar to that found in severe diabetes—a high fasting blood sugar and an extreme elevation of



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blood sugar after the ingestion of glucose. In these animals, the lymphopenic response ran parallel to that of the normal animals although set at a lower level presumably because of the influence of the high blood sugar levels. The findings are similar to those reported in human diabetic patients reported by Marks, Marks, and Jailer(17).

Since it was now evident that the lesser lymphopenic trend found in half the patients was due to adreno-cortical deficiency, a study was now undertaken of other biochemical variables which might serve as indicators of adrenal reactivity. These included the urinary uric acid, sodium, potassium, 17-ketosteroids, and corticosteroids. Glucose tolerance tests were conducted in 41 normal men

TABLE 2

MEANS OF PERCENTAGE CHANGES FROM CONTROL  
VALUES IN URINARY VARIABLES IN 41 NORMAL  
SUBJECTS AND 36 SCHIZOPHRENIC PATIENTS

Variable	Subjects	1 hr.	3 hr.
Uric acid .....	Normal	+ 52 *	+ 10 †
	Patient	- 3	- 12
17-ketosteroids .....	Normal	+ 31 †	+ 33
	Patient	+ 9	+ 11
Corticosteroids .....	Normal	+ 2	- 18
	Patient	+ 23	+ 3
Potassium .....	Normal	+ 12 *	- 31
	Patient	- 17	- 38
Sodium .....	Normal	+ 30	- 4
	Patient	+ 19	+ 2

\* Difference between normal and patient means—signifi-  
cant.  
† Difference between normal and patient means—border-  
line significance.

and 36 male schizophrenic patients, aged 20-40. The mean age of both the normal and patient groups was 32. Approximately one-half of the patients had been hospitalized for not more than one year, whereas in the other half the period of hospitalization extended to as long as 17 years. The mean for the whole group was 3.2 years.

The percentage changes in the variables studied are shown in Table 2. The urinary collections were made during the 2-hour interval preceding the test and at 1 and 3 hours after the ingestion of the first dose of glucose.

The ingestion of glucose results in the normal individuals in a marked increase in the excretion of uric acid, of a moderate increase in the case of 17-ketosteroids and sodium, and a mild increase in potassium

at the one-hour point. The patients show a mild increase in the excretion of cortico-steroids and sodium. The percentage increase is significantly greater for the normal subjects than for the patients in the cases of uric acid and the potassium ( $p=.01$ ) while in the case of the 17-ketosteroids the difference is on the borderline of significance ( $p=.03$ ). At 3 hours, the values subside to or below the control levels with the exception of the uric acid and the 17-ketosteroids. Here, only the uric acid value shows a possibly significant difference ( $p=.03$ ) between the 2 groups. No relationship was obtained between the subtype of schizophrenia and the magnitude of the responses. There did seem to be a slight relationship with duration of hospitalization, the acute cases (of less than one year's duration) showing an average change at the one-hour point 13% higher for all the variables than did the more chronic group.

In general, it may be said that the administration of glucose acts as a general stimulant to many phases of adreno-cortical activity and that schizophrenic patients on the whole show a lesser response than do normal subjects.

DISCUSSION

From the foregoing data it is evident there are abnormalities in the carbohydrate metabolism and adreno-cortical reactivity of a high percentage of schizophrenic patients. While the exact physiological mechanisms responsible for these phenomena are as yet not clear, the hypothesis may be offered that the emotional disturbances affect the adrenal cortex via the anterior pituitary to accelerate the breakdown of protein to produce an excessive amount of glucose once the exciting mechanism is set by the ingestion of carbohydrate. Since the test procedure is indicative of the fact that prolonged hyperglycemia results from the ingestion of food, the question must be raised as to whether the elevation of blood sugar levels is entirely innocuous or interferes in some way with other enzymatic relationships within the organism. In a recent article, Gass, Cherkasky, and Savitsky(18) note the fact that the ingestion of excessive amounts of carbohydrate results in a fall in serum potassium with possible resultant effects on the release

of acetylcholine and the resynthesis of choline acetylase, mechanisms important in the transmission of the electrical impulse along nerve fibers. This problem is particularly pertinent in relationship to the central nervous system whose sole source of energy is carbohydrate.

The relationship of the adreno-cortical deficiency to the psychiatric status of the patients is as yet undetermined. We do not know whether this deficiency is the result of initial atrophy or due to exhaustion because of repeated stimulation from the mental tension incident to the psychosis. In relationship to this point we may recall the Rorschach findings on the patients with reduced sugar tolerances, *i. e.*, that they are under more tension or are capable of less control than the others. At this time we may say that since abnormal sugar tolerances are found as commonly in the chronic as in the acute cases, it may indicate that there is more emotional disturbance going on in the average chronic schizophrenic patient than is ordinarily assumed. It is possible, therefore, for the endocrine factors to become exhausted. On the other hand, the lack of responsivity of the patients may be considered as a special type of adaption insulating them from any stresses that may be placed upon them.

It is also of interest to speculate on the importance of this hypo-adreno-cortical reactivity to the relative refractoriness of schizophrenic patients to all forms of therapy. It should be said at this point that the patients in whom the adreno-cortical studies have been carried out are a select sample. In the first place, they must be fairly cooperative in order to satisfy the technical requirements of the test procedures. In the second place, they include a high percentage of cases with a long period of hospitalization. Thus, the findings may be quite different in an acutely disturbed group of patients. Further research is going on in this regard.

The correction of the adreno-cortical deficiency has been attempted by the administration of desoxycorticosterone acetate to a few patients. No changes were evident in the psychiatric status. A more optimistic light has been thrown on this possibility by the observations of Hench, Kendall, Slocumb, and Polley(19), who noted eu-

phoric states in arthritic patients to whom large amounts of an adreno-cortical hormone (compound E) had been administered. The possibilities of this substance in the field of mental disease await further investigation.

#### SUMMARY

A series of studies have been carried out in schizophrenic patients and normal controls that indicate that (1) there is a reduction of tolerance to glucose in this psychosis; (2) the response of the adrenal cortex to stimulation by the ingestion of glucose is generally deficient as exemplified by measurements of various blood and urinary variables known to be pertinent to adreno-cortical activation.

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## STUDIES OF ADRENAL CORTICAL ACTIVITY IN PSYCHONEUROTIC SUBJECTS<sup>1</sup>

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The rapidity with which findings in the field of endocrinology are being extended into psychiatry is both gratifying and startling. Prior to the war satisfactory studies of variations in adrenal cortical function in man were practically confined to observing the extremes of deficit and of overactivity, as represented by Addison's disease, on the one hand, and by Cushing's and allied syndromes on the other. Animal experiments indicated that physiological variations in function of the adrenal cortex occurred in response to a variety of stresses. The development and the application of new techniques were necessary before it was possible to measure in man changes in adrenal cortical function that might be characterized as falling within physiological limits. Changes within these limits have received our recent interest and attention. The psychological implications of such changes still remain to be properly explored.

### METHODS

The subjects used in these studies were patients in this Institute or members of the staff. As criteria of adrenal cortical activity the following group of indices has been employed in all subjects: (1) an increase in circulating neutrophils, (2) a decrease in lymphocytes, (3) a decrease in eosinophils, and (4) an increase in the ratio of urinary uric acid to creatinine. The subjects most recently studied have been investigated also with respect to the excretion of (5) potassium, (6) sodium, (7) 17-ketosteroids, and (8) neutral reducing lipids (corticoids).

<sup>1</sup> Read at the 105th annual meeting of The American Psychiatric Association, Montreal, Quebec, May 23-27, 1949.

From the Department of Psychiatry, McGill University, and the Allan Memorial Institute of Psychiatry.

This work was done with the aid of a grant from the National Research Council of Canada.

Our thanks are due to Dr. John R. Mote of the Armour Laboratories for supplies of ACTH.

The methods used were those employed currently by workers in this field.

The possibility of establishing a dose-response curve for each index of adrenal cortical activity separately, and more particularly, for all of the indices combined together in some practical manner has been considered. If this were possible, a basis might be supplied for estimating the physiological effect of any stress that elicited an adrenal cortical response. This possibility is still being explored, and the following is a rough outline of our progress so far.

In attempting to summarize our data for easy communication we have had to consider 3 difficulties: (1) Such indices as we have used provide a rather unwieldy mass of data; (2) small changes in any index are relatively insignificant; (3) different indices, determined on the same subject, at the same time, may not agree as indicators of adrenocortical activity. This last is hardly surprising when one considers that the determination of any one index may be subject to a variety of possible errors, and that all factors involved in a change or lack of change are not yet understood. It seemed, therefore, that whether or not there had been a change in the activity of the adrenal cortex might be more definitely determined by the concurrent consideration of as many indices as practicable. To replace a forbidding mass of data by a simple, yet relatively quantitative expression that might, at the same time, combine the information from the several indices and deal only with changes large enough to be relatively significant, we have determined a combined index in the following manner. The amount of change in several types of experiments on normal subjects and patients has been plotted and divided somewhat arbitrarily into 4 classes: no change, mild, moderate, and marked. These classes have been given numerical values: 0,  $\frac{1}{2}$ , 1, and 2. The limits of each class were based on a study of the data of Thorn *et al.*, of the Worcester group, and of our own studies.



Table 1 lists the limits of each class for each of the first 4 indices of adrenocortical activity mentioned above. The amount of change in each index is expressed as the percentage change from the pretreatment level of that index. The classes may be roughly characterized:

Class "zero"—the degree of change usually found in normal individuals engaged in ordinary, rather sedentary daily work. A definite mild stress or a small dose of ACTH always gives a greater response in a normal subject.

Class "one-half"—a degree of change rarely found in normal individuals at non-stressful work and less than that caused by small doses of ACTH.

Class "one"—the range of change common in stress or following a dose of ACTH not exceeding 25 mg.

## RESULTS

The work to be reported here is in a preliminary stage and only tentative conclusions can be drawn from the data. However as our investigations are extended we hope that more definitive answers may be realized.

1. *Adrenocortical Reaction to Injections of ACTH.*—Thirty-three subjects have been given injections of ACTH (Armour) in doses ranging from 2.5 to 25 mg. equivalent of the Armour standard. Three subjects have received more than one dose level. Of the entire group, 3 were schizophrenics, and the rest psychoneurotics. Fig. 1 illustrates the dose response curve in 3 subjects. As one might have anticipated, the response is greater with increasing amounts of ACTH. There is, however, a wide variation in the 3 patients in the degree of response obtained at a dose of approximately 10 mg. Fig. 2

TABLE 1  
PERCENTAGE CHANGE IN EACH CLASS

Index	Class numbers			
	0 Less than	$\frac{1}{2}$ Between	1 Between	2 Over
Neutrophil increase .....	20%	20-50%	50-150%	150%
Eosinophil decrease .....	15%	15-20%	20-70%	70%
Lymphocyte decrease .....	15%	15-20%	20-35%	35%
Uric acid/creatinine increase.....	45%	45-60%	60-150%	150%

Class "two"—a greater degree of change than is usually noted after 25 mg. of ACTH.

As more data become available it is highly probable that the limits of these classes will be revised. In any instance the sum of the class numbers gives a cumulative index with a value from 0 to 8.

## PROBLEMS

The following problems concerning adrenocortical function have received our attention:

1. Adrenocortical reaction to injection of small doses of adrenocorticotrophin (ACTH).

2. Adrenocortical response to (a) injection of saline and venipuncture, (b) thermal pain test.

3. Adrenocortical activation with electroconvulsive therapy (ECT).

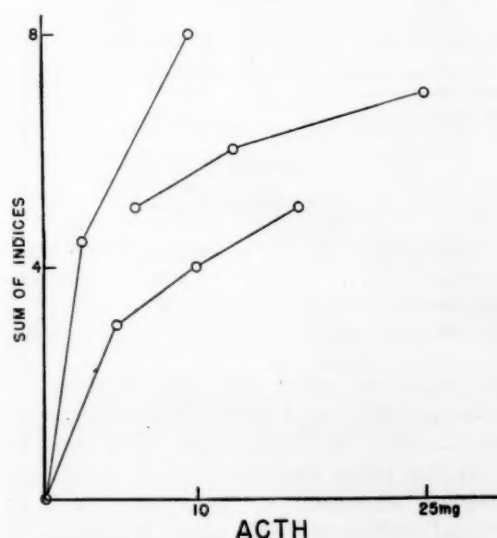


FIG. 1.—Dose response curves in 3 subjects.

shows the response obtained in the other 30 subjects plotted against the dose of ACTH

used. The cross-hatched circles represent the 3 cases of schizophrenia; the closed circles, the psychoneurotics. The response indicated by these data is qualitatively similar to that reported by other workers in allegedly normal subjects. Whether psychoneurotic patients are less or more sensitive to ACTH than normal individuals we

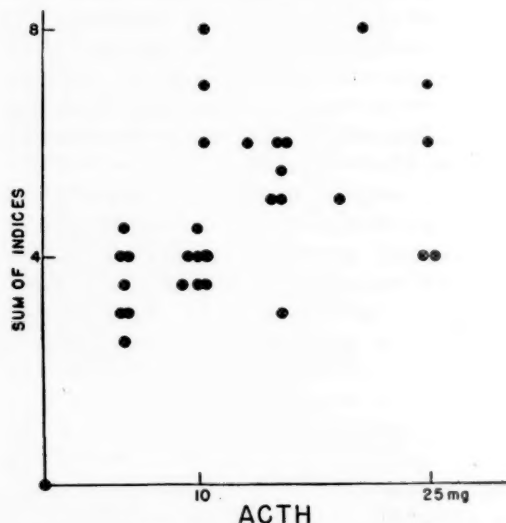


FIG. 2.—Responses of 30 subjects to one dose of ACTH (see text).

TABLE 2  
POTASSIUM

Dose ACTH	No. of cases	Interval	P
5.2 mg. ....	7	1-3 hr.	.06
10.4 mg. ....	6	3-5 hr.	.05
15.6 mg. ....	7	3-5 hr.	.02

TABLE 3  
NEUTRAL REDUCING LIPIDS

Dose ACTH	No. of cases	Interval	P
5.2 mg. ....	5	1-3 hr.	.05
10.4 mg. ....	5	1-5 hr.	.05
15.6 mg. ....	8	1-5 hr.	.01

are unable to state. The answer could be achieved only by a great deal more work than facilities at the moment make possible.

In the more recently studied cases, the rate of excretion of potassium and of neutral reducing lipids after injections of ACTH has been compared with the rate after injections of saline. This difference in rates seems to be significant, as shown in Table 2 for potassium, and Table 3 for neu-

tral reducing lipids. Table 3 shows that in this rather limited series the significant difference in the rate of neutral reducing lipids seems to have been obtained with a dose of ACTH as low as 5 mg.

2. *Response to Test Situations.*—In the foregoing section it has been demonstrated that psychoneurotic patients respond to ACTH. It was important to determine to what extent the experimental situation might cause an endogenous discharge of ACTH. The following experiments have provided at least partial answers.

(a) *Response to saline:* Each of 22 subjects who were given ACTH was given also an injection of saline and had blood samples taken in a program practically identical with that used in the study of ACTH. They did not know the nature of the injection. Most of the cases in this study had anxiety. An attempt was made to assess the degree of tenseness and anxiety during the conduct of the test and this was characterized as mild, moderate, or severe. In Fig. 3 the cases are grouped according to the degree of apparent anxiety; the level of the circles indicates the degree of adrenocortical response as expressed by the sum of the indices; the open circles refer to the mild cases; the crossed circles, the moderate cases; the closed circles, the severe cases. From Fig. 3 one gains the impression that the degree of response to the test situation may be influenced by the severity of the patient's anxiety state. Hence it would seem unsound to conclude that all adrenocortical activity following an injection of ACTH is due solely to the injected material.

(b) *Pain test:* Other studies on the influence of controlled stress on adrenocortical function have been done in association with our colleague, Dr. R. B. Malmo. Variation in blood lymphocyte counts was used as the criterion of changed adrenocortical activity. The subjects were exposed to a control stress situation using the Hardy-Wolff thermosimulator. Blood studies were made before the test and 2 and 4 hours later; on another day control counts were made at corresponding times on each subject. The average percent change in lymphocyte counts, as shown in Fig. 4, indicates how definitely the stress decreased the number of circulating lympho-

the influence of corticosteroids on the variation of lymphocyte activity. Corticosteroid stress before and after another response percentage is shown in the stress lymphocyte

3. *Electroconvulsive Therapy*.—Our studies on the activation of the adrenal cortex by ECT support the findings of other investigators. Our earlier results, already reported before the Canadian Physiological Society, are summarized in Fig. 5. Here the height of the bars represents, for the number of patients indicated, the average value of

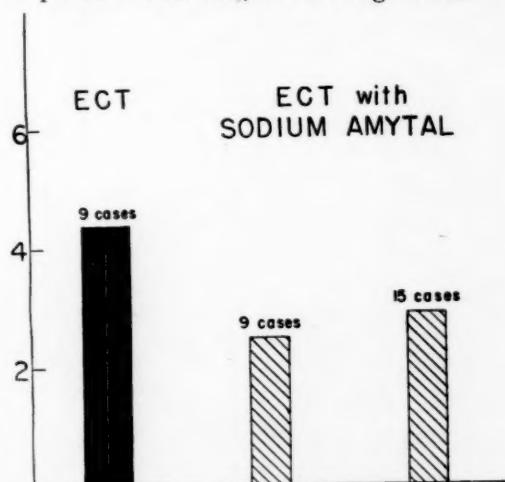
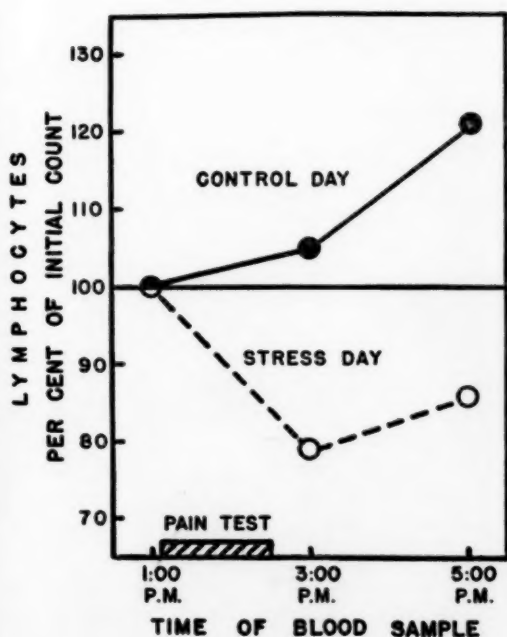


FIG. 5.—Effect of ECT on stress indices.



Whether or not the activation of the adrenal cortex has any influence on the clinical effectiveness of ECT is not yet apparent, in spite of a variety of speculations on the subject.

## SUMMARY

The use of a cumulative index of adrenal cortical activity has been described.

This has been applied to the estimation of adrenocortical activity after (1) small doses of ACTH in anxiety states, (2) injection of saline and venipuncture, (3) controlled thermal pain, and (4) electroconvulsive therapy.

In all these experiments the data indicate activation of the adrenal cortex.

It is suggested that the greater the patient's anxiety and tenseness the greater the activation of the adrenal cortex by the test situation.

The use of pretreatment sodium amytal seems to decrease the response of the adrenal cortex to ECT.

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## CONCEPT AND EXPERIMENTAL DESIGN IN THE STUDY OF STRESS AND PERSONALITY<sup>1</sup>

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Contemporary psychiatric research has advanced conceptually and methodologically beyond the boundaries assigned it by even its most enthusiastic supporters of only a few years ago. However, outside the therapeutic situation the clinician finds himself in strange and at times bewildering company. Often he is on the defensive and in reaction distorts his rôle in, and contributions to, the total effort. We would like to discuss the rôle of the psychiatrist and psychologist in the research field, particularly as it relates to concept and experimental design in the study of psychosomatic relationships.

The manipulation of the environment for the purpose of producing changes in the subject organism is the basis for much of our research. The interpretations we make of our data not only must relate to the quality of our experimental design, but for the clinician must have relevance in terms of a *concept of personality*. Changes occurring in the organism, regardless of their origin, can be defined under a concept of personality in terms of an organism-environment relationship. It is this relationship which we seek to understand in approaching the dynamics of personality including, as it must, psychosomatic relationships.

We are all aware of man as an organism attempting to survive in a complex of relationships involving his internal environment in terms of his own organization, a physically definable external environment, and the so-called social or cultural environment. The complexity of the conceptual schema required to include in a consistent fashion all the individual mechanisms necessary to account for the behavior of the organism is almost insurmountable. We must therefore

accept a rather basic viewpoint, namely, that we may successfully isolate a discrete mechanism, but we must see it as a convenient but limited abstraction. Its significance for the behavior of the total organism is primarily, if not exclusively, related to a particular frame of reference and beyond that provides only the basis for perhaps useful speculation.

This state of affairs need not lead to defeatism and the abandonment of basic research. Indeed, our present understanding of behavior already permits us to set up miniature subsystems that have explanatory power for certain classes of phenomena. One example is our present concept of anxiety, which can be dealt with quite effectively in terms of psychoanalytic theory or of neurophysiological theory. Both frames of reference are interpenetrating and contribute useful knowledge for either point of view. The danger lies in the attempt to explain the one in terms of the other in the absence of any concepts as yet consistent or broad enough to contain the disparate mechanisms and principles subsumed under the two miniature systems. Too often attempts at the construction of global concepts have either ignored the data of other disciplines or have been the product of an illogical and confusing eclecticism. Even as we recognize the desirability of a holistic biology we find that experimental investigation must, in the study of psychopathology, often be content to deal with limited and abstract constructs regarding particular functions in a behavioral sequence. It is in the failure to recognize this that much work in the field of psychosomatic relationships has gone astray, attributing to correlations between physiological and psychiatric data explanatory and predictive potentials they do not in fact possess. In our zeal for advancement under the ægis of "psychosomatic medicine" we find psychiatrists "doing physiology" and physiologists rendering psychiatric judgments.

<sup>1</sup> Read at the 105th annual meeting of The American Psychiatric Association, Montreal, Quebec, May 23-27, 1949.

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<sup>2</sup> Director of Research.

<sup>3</sup> Chief Psychologist.

The results in many instances have been dramatic, but hardly consistent with good experimental design.

We have not been entirely innocent of such indiscretions and will cite some of our own experimental work as a means of stating the problems involved. Our investigative team consists of representatives from a variety of scientific disciplines and backgrounds. If we all agreed that the study of the organism as an on-going unit under varying but controlled conditions was promising of fruitful returns, we soon discovered in our interpretations that we were not always talking about the same thing. This reexamination of our joint efforts has been revealing and we believe most useful. The following investigations were variously under the direction of different ones of us and consequently the original emphasis depended upon the particular persons involved. This meant that certain investigations were primarily physiological studies while others were more specifically studies of psychological phenomena. In either case we were interested in the implications of the one for the other.

#### DISCUSSION OF EXPERIMENTAL WORK

I. One of our early studies concerned the effect of a heat stress upon the autonomic nervous system(1). Schizophrenics and normals breathed through the mask of a standard BMR apparatus. After a given time the temperature and humidity of the oxygen were increased sufficiently to block the loss of heat from the lungs. None of the subjects was forewarned of the nature of the stress. It was found that the patient group was definitely less responsive than the normal subjects to the disturbance produced by the warm, moist oxygen, but the autonomic measures used did not differentiate the two groups during the prestress phase. In going back over this study it was found that the data on 11 of the 40 control subjects had not been included in the report because these subjects had begun to react very vigorously during the prestress phase and could not be continued in the experiment. None of the schizophrenics showed this reaction.

This finding directs our attention to the prestress phase of the study and a considera-

tion of the state of the organism at that time. Even though the data tempt one to conclude that schizophrenics are basically less reactive autonomically than normals, this generalization is too restrictive and fails to account for certain things seen in the normal group. For example, a further interpretation of the data that seems useful would emphasize the rôle of anticipatory set in preparing the subject to deal with new experiences. Is it not likely that the prestress set of the patients differed from that of the control group and that in the case of the normals this entailed attention to new and real stimuli, the perception of which prepared the individual to regard the continuance of the experience as threatening and dangerous? In many cases this apparently was enough to fire off autonomic responses of great magnitude and resulted in the withdrawal of the subject from the test before the intended stress was ever introduced. In the case of the schizophrenic the situation may have had little or no stimulus value in this frame of reference and both his immediate and later responses may have been tempered by the quality of his set and interpretation of the situation. A crude but appropriate analogy is offered by the foot-race between a normal and a schizophrenic. Midway in the race the patient stops to gesticulate at the sky and the normal speeds across the finish line. Can we from this make judgments about the comparative running ability of the contestants?

II. To study the idea offered above an investigation(2) was undertaken which seems to corroborate our interpretation. In this procedure the subject lies comfortably on a cot in a quiet room. He is told that at some time a buzzer will be sounded, but he is to do nothing about it. Before sounding the buzzer the experimenter forewarns the subject by saying "ready." The galvanic skin response recorder is running continuously throughout these procedures. When the word "ready" was given, normal subjects reacted three times as strongly as the patients, but both groups reacted about the same to the buzzer itself.

From these data we could conclude that schizophrenics show a deficit in the establishment of an environmentally oriented set

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when the external stimulus does not possess significance for them. The signal "ready," because it was meaningful to the normal subject, evoked changes which structurally and functionally belonged to the stimulus. Further examination of the data revealed that when anticipation was not a factor the schizophrenics and normals reacted similarly.

III. The learning of a task is regarded by most people as involving some form of stress for the organism. It was our desire to compare the learning ability of schizophrenics with that of normals under two sets of conditions: (1) when the only apparent stress is the task of learning, and (2) when this task is interfered with by the addition of other stressing conditions. In this study(3) the subjects operate an airplane-type pursuit-meter. By means of manipulation of the controls they are able to track down and sight on an enemy plane which is projected on a screen and which moves about in random fashion. The rate of learning to manipulate the controls is measured by the curve of increased percent time on target. The additional stress is provided in the form of sudden noises, blasts of air, light flashes, and bursts of sparks. These are presented at random except that they cannot occur as long as the subject is "on target"; thus he has a measure of control over them and for most subjects this becomes a rather exciting game. After a period of operating the pursuit-meter under these conditions the extraneous stimuli are omitted and the subject again proceeds as he did in the prestress phase. The learning curves of the prestress and poststress phases are then plotted and a comparison can be made for the individual subject against himself or of groups of subjects.

In the prestress period our patients and normals learned at approximately the same rate. Following the stress period the schizophrenics practically stopped learning while the normals continued to improve albeit at a somewhat slower rate. Here again the temptation to arrive at a simple conclusion is great, namely, that the schizophrenic cannot operate as efficiently under stress as normals. We might elaborate upon this to the extent that we could say that the schizophrenic fails because he has not the neuro-

physiological resources which could provide the extra energy needed to meet the stress situation. A partial answer to this statement was provided by our investigators(4) in a study of the effect of this learning task upon the glucose tolerance curve. They found that this task produced a shift in the form of the curve from a normal to an abnormal curve in both schizophrenics and normals alike. Here, then, we find a task which differentiates the 2 groups behaviorally, but not physiologically at least as far as the glucose tolerance is concerned. Since the prestress learning rate was the same for both groups and since the effect of stress on the glucose tolerance was approximately the same, we must account for the difference in learning in the poststress period along somewhat different parameters.

We are inclined to ask what the stress stimuli mean to the subjects and very likely differences of interpretation and evaluation are operating. Normals can accept the noises and sparks as part of a game and impart to them a kind of reality they do not in fact possess, but which nevertheless does not get out of control. Their externally oriented sets keep them sufficiently motivated to play the game out and their limited apprehension of the stress stimuli, while affecting their learning efficiency, does not stop it. The schizophrenics, dealing more concretely with these stimuli, may accept them for what they are and as such find them annoying or distracting, or they may actually regard them as real threats independent of the context of the task. Behaviorally, the evidence is that they were more sensitive to the stress than normals. This is not necessarily a contradiction of the opinion that schizophrenics are less responsive than normals, but rather demands that we avoid the uncritical acceptance of such as a generalization and deal more precisely with specific conditions as the data demand. It may well be that different techniques of adjustment utilize different mechanisms and that the choice of adjustive behavior is determined by the particular characteristics of the given organism and the particular meanings a given situation has for him. We must remember that what we are obtaining as data are a series of arbitrary endpoints (whether physiological or beha-



vioral) any one of which may be dependent upon mechanisms that are qualitatively different for normals in contrast to schizophrenics. The problem is expanded from the mere question of "responsivity" to "responsivity to what and how." The response of the organism to our designated stimulus is not simply the resultant of a chain of reactions determined by fixed quantities of participating elements as in a chemical reaction. We are involved with values, meanings, motives, needs, and the further complicating fact that the organization of a response has in itself stimulus values which may be qualitatively and quantitatively independent of our designed context of the experimental situation.

IV. These observations are supported by a study(4) in which the character of the glucose tolerance curve of our psychotic group was compared with their Rorschach records. It was found that the greater the evidence of control (over spontaneous expression and impulsivity) as measured by the Rorschach the more normal the glucose tolerance curve. Where control was deficient the glucose tolerance was also impaired. We cannot say definitely that the one is a result of the other. Both may themselves be dependent upon a still more basic condition or mechanism. We are inclined to assign a degree of primacy to the psychologically defined control mechanism mainly because we feel it unlikely that reversing the glucose tolerance curve would strengthen control as measured by the Rorschach.

V. Those of us who have been interested in the behavioral characteristics of our patients were aware of the inadequacy of our tools for the accurate study of such phenomena and also how difficult it was to attempt the correlation of clinical observations with the data of other disciplines. The Clinical Psychiatric Rating Scale(5, 6) was devised to meet these needs. It consists now of 22 items that can be studied both qualitatively and quantitatively. Recognizing that these in themselves are abstractions and constructs, at least we have had the means of testing certain hypotheses; in essence, that mental disease or maladjustment manifests itself in the behavior of the patient and that significant changes in the course of the dis-

ease can be described in terms of degree and direction as they occur in certain previously defined components of behavior.

The actual use of the scale has served to fortify a basic attitude on our part, namely, that we cannot speculate about mechanisms without classified data derived from the observation of, and communication with, the subject patient. A discussion of psychosomatic relationships that ignores phenomenological evidence is as empty as what Kant referred to as concepts without percepts. With the use of the scale the patient is his own control and it is the alteration of his particular behavior patterns which we study. We want to know what functions are disturbed and how much, not does he have schizophrenia and how much. In future studies of stress we shall be interested to see if there are behavioral criteria and if these will correlate in any way with physiological or psychological data.

VI. Out of our general interest in the behavior of patients have evolved a series of studies of what we call language behavior. Some of our experiences in the course of developing our techniques are pertinent to this discussion.

In one test(7) the patient is presented a series of simple part-figure drawings which he is asked to identify as quickly as possible. One of these pictures is quite obviously an automatic pistol. A male schizophrenic responding fairly quickly said, "That's a boy." When asked to explain, he stated, "It rejects. It never receives." We could have been content with the pursuit of such associations, but on a hunch we asked, "What do you really see?" Quite casually he replied, "Oh, that's a gun." With this kind of response we can no longer concern ourselves merely with an analysis of associations in terms of meanings or formal qualities. We cannot generalize comfortably by saying schizophrenics think concretely or paralogically. This patient did everything a normal did, plus a great deal more. Our attention is directed perforce to questions regarding perception, control mechanisms, motivation, and others. Why did he make the original response, knowing all the time what the stimulus object was? Was it a stressful stimulus, a threat? One gets the

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feeling that this patient like the poet or painter experiences all that we do plus much more, obtaining meanings and inferences which our very normality prevents us from recognizing. If this be true then the personally determined evaluation by the patient will be a powerful factor in his reaction to any manipulation of the environment which we might make, and our estimate of the potency of the stimulus cannot be isolated from the particular responding organism. In the absence of a concept of personality such phenomena would be meaningless and unapproachable experimentally.

In a related study (8) the subject is presented a series of words. With the presentation of each word he is to make up a sentence using the word and do so as quickly as possible. As would be expected, the patients generally have longer response times and produce more bizarre sentences than normals. However, some patients respond more quickly and with better organized sentences to some words than do our normals. In response to the word "pull" a control subject gave the sentence, "There were three Pullmen." In response to the word "above" one person said, "The machine is above the glass door," while another said, "The sky is above us." Which was the paranoid patient? It was the latter.

Our data thus far reveal not only differences between patients and normals, but what is more important, two kinds of overlapping similarities: (1) patients with "normal responses" and (2) normals with "abnormal responses." This in itself does not come as a surprise, but accounting for them experimentally for the understanding of phenomena in terms of health or disease is extremely difficult. Between the presentation of the stimulus and the response of the patient a complex of interpenetrating functions goes into operation, and obviously we cannot use the response itself as an explanation of the mechanisms involved. It is precisely this form of problem which has been present in so much of research in psychosomatic relationships. As far as this particular study is concerned we would like to know what is going on in the patient who takes an unusually long time to respond to the given stimulus word or who makes a bizarre re-

sponse. Do the physiological concomitants of such events reveal explanatory differences between normals and psychotics? Why can schizophrenics speak in normal fashion at one moment and not at another? Whatever the answers may be they cannot be completely isolated from some consideration of a wide range of psychosomatic functions.

VII. Beyond the consideration of individually determined factors in the life of each patient are those broader cultural influences which are not yet clearly definable, but which appear to play a rôle in such matters. We have recently encountered evidence thereof, though we cannot state it with any great degree of assurance. In the period 1942-43 a group of 43 male veterans were admitted to the hospital (9). At the end of about a year they were classified according to a number of items. These included such general matters as to whether they were in or out of the hospital, their clinical condition, and personality characteristics. This year a second study of the same group was undertaken, in part to see whether or not the groups had altered significantly. As far as their being in or out of the hospital was concerned, or whether they were better or worse clinically, certain data stood out. We found that the number of patients in any one of these groups had remained about the same, but the individuals comprising these groups had shifted extensively from one group to another. In brief, the population volume of each class had remained stable while the units comprising them had interchanged freely. If this phenomenon is borne out by studies on larger and more heterogeneous groups, we shall have to examine very critically the possible cultural factors operating to influence hospital population size and adjustment to (or acceptance by) the extrahospital environment. The meaning of stress and disease cannot in this situation be divorced from what appear to be very general but effective social forces.

#### COMMENTS AND CONCLUSIONS

We have attempted, albeit in a somewhat circuitous fashion, to point up the kinds of experiences in the conduct of research that have led us to a critical reexamination of our

concepts and experimental design in the field of psychosomatic relationships. In closing we wish to comment on the rôle of the clinician in this area of investigation and to make several recommendations derived from our own struggles for those who would participate in such work.

In the hospital and in the clinic it is the clinician who must estimate the order and severity of the patient's illness, select and administer therapy, and attempt to predict his future adjustment capacity. No matter how much or what kind of information is afforded him from other sources he must work directly with the patient in a rather specialized relationship. His powers of observation plus his shared experiences with the patient enable him to make those judgments that determine the ultimate evaluation of the case. It is the synthesizing quality of his observations, related as they are to the empathic bond between physician and patient, that is the singular advantage he possesses over all other techniques available for the study of the patient. It is also the basis for certain disadvantages and for the particular prejudices of psychiatry in the field of research. A major disadvantage lies in the subjective quality of much that enters into the formulation of these "synthetic judgments" and the difficulty one has in abstracting them to such a point that they may be treated as logical inferences from classifiable data. The clinician attaches value, meaning, and predictive significance to phenomena expressed behaviorally. It is necessary and proper that we do so even as we recognize that in so doing we may for the time being make it more difficult if not impossible to arrive at those epistemic correlations with the data of physiology that might lead to the global concepts we desire. We cannot fall back upon the constructs of physics and chemistry and do justice to the kinds of judgments it is ours to render.

In our introduction we stated that for us a concept of stress has relevance in terms of a concept of personality organization. Essential to any concept of personality dynamics, whether it be expressed in terms of psychoanalytic, topological, or Hullian mechanisms, is the viewpoint that behavior

is motivated and occurs when a need, drive, or tension state exists in the organism. Without belaboring instinct theory we are reasonably secure in positing the existence of certain conditions in the organism that we may call tension states. These originate in disturbances of homeostasis, but with learning and maturation they come to operate effectively in the absence of immediate tissue requirements and ever more in a qualified relationship with environmental conditions. In response to these tensions we develop techniques of adjustment the aim of which is to reduce them to subthreshold levels. For the clinician, behavior, whatever its qualities may be, is a manifestation of change in tension states. The attributes of these tension states are dependent variables not only of the given stimulus, but of the prepotent characteristics of the total organism as the emergent, on-going product of his experiences operating in and through the physiological matrix by means of which he occupies a position in a space-time field.

This being true, then collaborative research is by definition necessary for an ultimate understanding of human behavior at any or all levels. In our experimental design each of us shall, despite our differences in viewpoint, critically define three phases of the study as elements within a structured whole:

1. The stimulus—its form, magnitude, and meanings.
2. The mediating mechanisms within the organism—not the organism as a whole.
3. The response—its quality and quantity as a function of the stimulus and the mediating mechanisms.

Because of our differences any experiment will yield discrete sets of data which have significance primarily in an equally discrete frame of reference. In our zeal for holistic concepts we must guard against two tendencies:

1. The premature attempt to "explain" psychiatric phenomena in terms of physiologic data (and vice versa) on the basis of statistical correlations alone.
2. The tendency to ignore the data of our colleagues because we cannot translate them conveniently to our special needs.

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As each discipline develops its own conceptual framework more adequately the kind of interpenetration we desire will occur and then we shall see emerge those unifying concepts necessary for a true science of human behavior.

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## THE PSYCHOSOMATIC CONCEPT IN WORKING CLOTHES<sup>1</sup>

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Fort Thomas, Ky.

The psychosomatic concept with all its implications swept the public consciousness when veterans emerged by the hundreds from the war physically damaged, occupationally inept, and emotionally disrupted. It sounded the call for all-out rehabilitation, for treatment of the "whole man," for multiple therapies—physical, corrective, psychological, occupational, and educational. Grateful fellow citizens strained to meet the challenge to human rebuilding and to pay off their debt to the nation's veterans.

Perfection in handling the problem was not claimed in those earlier days. The need was immediate and urgent, and the best was done that could be done with the time and facilities afforded. It was and is heartening to know that modern rehabilitation measures returned to their communities substantial numbers of debilitated men as useful and self-sustaining citizens.

It is human nature to draw reassurance from our achievements, however, and to suppress our failures for consideration under more fortuitous circumstances. Lest we suppress too long and thus lose consciousness of our inadequacies, attention is called to the recession of both the emergency and the necessity for makeshift. The time is here to revise and to refine. It is time to acknowledge the depressing numbers of veterans whom rehabilitation measures have not helped, who are weighting down the taxpayers in large and increasing numbers and who, if not helped promptly, will come to burden the public in alarming proportions.

These men are a challenging problem for which there is doubtless no single explanation. It is proposed, however, that significant responsibility lies in the fact that the psychosomatic concept has not yet been put into full working operation. The *integrative*

note, intrinsic in the concept, is defective in application. Staff functions of most rehabilitative centers are prone to be additive, supplementary, part-to-part, and therefore, incomplete.

The defects in integration are apparent in two ways: (1) in the too-frequent ignoring of important psychological aspects and (2) in the loose organization of staff operations.

The first type of defect refers to present-day minimizing of psychological forces which, of course, can never be divorced from physical, vocational, or any other human operations. As a matter of fact, every treatment specialist, whether or not psychologically trained, of necessity evaluates his patient's intellectual and personality qualities if he is to achieve any goals at all. This he does during the process of treatment—toward the close of which he can tell a fair amount about his patient's surface adjustments. He acknowledges, ordinarily, that he could have done a better job with economy of time and effort had he known these facts and more, at the beginning of treatment. The neuropsychiatrist and clinical psychologist, however, are still traditionally obliged to keep "hands off" unless the patient happens to present a "psycho" label. They remain dignitaries in a cubbyhole with no established place in planning the training programs for any but the "psychos"; or in providing guide posts for supportive therapy for any but those classified with psychiatric diagnoses. The mechanical arts therapist works with his patients as relatively unknown quantities, and so do the corrective and other therapists. Educational specialists plead that other patients, too, have potentials, limitations, and assets, and what of them? But not yet have the psychiatrist and clinical psychologist been released from conventional restrictions, and, in general, the privilege of "whole thinking" service is restricted to the patient formally classified as a psychiatric case. The same dichotomous thinking would lead, ipso facto, to the restriction of physical

<sup>1</sup> Published with permission of the Chief Medical Director, Department of Medicine and Surgery, Veterans Administration, who assumes no responsibility for the opinions expressed or conclusions drawn by the authors.

<sup>2</sup> Veterans Administration Hospital.



work-ups to only nonpsychiatric cases, and the practice of routine medical service in mental hospitals would be abandoned as unimportant.

The second type of defect refers to the diffuseness or lack of coherency in the handling of a case, and this runs through the processes of diagnostics, of planning, and of the therapy itself.

I. *Diagnostics*.—The need for integration of diagnostic findings has been emphasized repeatedly by present-day workers, for all processes to follow can be little better than the adequacy with which the case was comprehended. In some hospitals, though the practice is rare, very little integration is achieved. The most prevalent custom is the holding of staff conferences wherein diagnosticians and therapists confer on findings in order to gain a comprehensive understanding of the case. Their findings are integrated on-the-spot with or without stenographic recording. The policy presents distinct limitations, however, in that the time devoted to such conferences is necessarily limited, the direction loose, and evaluations and resultant plans are hasty and generally incomplete. Much discussion that is sound is lost in irrelevant discussion, more often than not never to be recollected in the actual conduct of the patient's rehabilitative program.

II. *Planning*.—Diffuseness and incompleteness of planning is not unknown—as recognized by patients and rehabilitation workers alike, and this is inevitable if the diagnostic process is inadequate. Further, planning is also time-consuming, requiring a considerable measure of analysis, integration, and original thinking to be effective. On-the-spot planning, which is the prevailing method, operates against this type of thinking, and its effects are seen in the fact that most therapeutic units operate on their own with few or no guides of therapeutic value.

III. *Therapy*.—The process of therapy is partly a test of the adequacy of diagnostics and planning. Ideally, every patient's assignments are suited to his needs, and therapists are equipped with guides and instructions for propelling each patient purposefully and progressively toward optimal rehabilitation. Few would dispute that the ideal is still some distance from reality. The trial and error

process, disappointments, and time-wasting activities are still excessive, and patients complain of feeling neglected and purposeless within the system.

There is no question of the soundness of the psychosomatic concept. The holding of a concept and the supplying of facilities to support that concept, however, still do not cure the man. In general, the integrative effort appears still defective, and the correction appears to be in (1) the extension of psychiatric-psychological services to all types of cases, and (2) greater coherence in the progressive handling of cases.

With the above corrections in mind, the Ft. Thomas Veterans Administration staff submits its interpretation of the psychosomatic concept in action through its three-step process, as follows:

*Step I—An Integrated Diagnostic Study*.—This study is a final, refined one, available to every patient, pooled from the findings and conclusions derived in contributing studies. Its function is to assemble, analyze, and integrate the medical, psychological, social service, and educational-occupational findings, to interpret their interactions, and to draw salient conclusions from them. The study is prepared tentatively by the clinical psychologist, to be followed by consultation between the neuropsychiatrist, clinical psychologist, social worker, and vocational advisor. A final report is then prepared in a "Psychosomatic Summary," containing the results of the study, with strengths, weaknesses, and potentials indicated. While the preparation of this summary is time-consuming, it is believed in the long run to be more economical and effective than are on-the-spot planning procedures which are prevalent today. The psychosomatic summary is therefore prepared carefully for permanent record—all of this preparatory for the second step in the application of the psychosomatic concept.

*Step II—Controlled Planning*.—Guided by the needs of the patient as indicated in the preceding study, plans are laid tentatively, to be revised or extended by the consulting group. These plans for the hospital program are then incorporated into the psychosomatic summary for presentation to the entire rehabilitative staff for discussion. The

final disposition of the case for rehabilitation is then voted on, subject to the approval of the chief medical officer. Plans include prescription assignments to rehabilitative divisions, designated in order of primary importance. Some type of physical therapy is usually necessary for the development of a "whole functioning" man. However, the pivotal point of the patient's complaints and the depth of his needs determine which type of therapy is primary. In some cases, the physical problem is most important; in others, emotional or educational-vocational problems take precedence. Timing problems are considered also in the construction of plans. For instance, a patient requiring occupational therapy may be so gravely debilitated physically that he is unable to avail himself of vocational services until his medical problems are partially resolved; or psychiatric problems may be most urgent, requiring partial resolution before the patient can cooperate within the rest of his rehabilitative framework. Such considerations as the foregoing enter into the treatment plans, as well as guides that are specific respective to rehabilitative departments. Rules for supportive therapy in all departments are also incorporated. At this point a therapist who has previously established good working rapport with the patient is appointed to sponsor him throughout rehabilitation.

*Step III—Therapy and Follow Through.*—Equipped with the knowledge necessary for comprehension of the veteran's problems, and with plans and objectives clearly defined, the therapeutic team sets in motion the "whole treatment" program, geared to the patient's needs. This program engages two broad types of service: (1) assigned areas of therapy as indicated in the psychosomatic summary; (2) sponsorship service which provides follow-through support in the process of attaining rehabilitative goals. At Fort Thomas the assigned sponsors are psychological trainees,<sup>3</sup> operating under the

<sup>3</sup> Ph. D. candidates in psychology.

supervision of the chief clinical psychologist and chief neuropsychiatrist. Under the sponsorship program, the assigned therapist makes it his business to know intimately the problems of adaptation his patients are undergoing. He evaluates constantly the adequacy of the plans as they are carried out, being ready to recommend changes or adaptations within the program as the need becomes apparent. He confers with the therapists, consults progress notes, watches the patient's setbacks and advancements; studies his habits of work, of thinking, of relating to people, of self-regard; and seeks to aid in correcting the habits that obstruct progress. As the physician makes ward rounds, the psychological sponsor likewise makes his rounds of therapeutic units in physical, education, and occupational areas. In short, he attempts to identify himself as closely as possible with all aspects of the case for the insight necessary to guide or to counsel. Thus informed, he holds weekly therapeutic conferences with his patients, operating on whatever therapeutic level is designated by the control therapist. The "Sponsorship Program" at Fort Thomas is a new and challenging responsibility of the Department of Psychological Medicine, constituting the "follow-through" which necessarily follows a set of plans.

A psychosomatic summary is presented below to illustrate the three working steps of the "whole thinking" concept at Fort Thomas. This patient had no psychiatric label on admission, but the findings disclosed through psychological-psychiatric study were highly significant in the conduct of the case. The summary is presented as free of technical terminology as possible in order that all therapists, regardless of type of professional backgrounds, can easily comprehend its contents. Psychiatric terminology particularly is held to a minimum in discussions and recommendations.

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PSYCHOSOMATIC SUMMARY

CASE No. 114. Male, white, age 29.

*Transfer Diagnosis.*—Thrombo-angiitis obliterans (Buerger's disease) of the lower extremities with bilateral amputation below the knee.

*Statement of Problem.*—To determine optimal rehabilitative program.

Reports

Critical Findings

- |                                |  |
|--------------------------------|--|
| Medical .....                  | 1. Bilateral leg amputation below the knee, secondary to Buerger's disease.  |
|                                | 2. Flexion deformity of left stump.  |
|                                | 3. Right leg adequately fitted, but some difficulty in fitting of bucket below knee.   |
|                                | 4. Pain in right hand and wrist; fluctuant tender swelling proximal to right wrist on ventral surface over ulnar side. Tenderness along shaft of middle and little finger. Some tenderness over palmar fat pads of hands. X-ray films reveal multiple tiny cystic areas in wrist bone, also possibly on shaft of right thumb just proximal to metacarpal phalangeal joint. |
| Psychiatric—Psychological .... | 1. Attention-getting—boisterous, falsely cheerful, petulant, irritable, demanding.   |
|                                | 2. Excessive internal stress which patient dares not reveal directly to others or to himself.  |
|                                | 3. Anxiety and depressive strains; antisocial urges; distorted self-regard. Potential for threatening, destructive behavior.   |
|                                | 4. Low average verbal ability; superior performance functioning.   |
| Sociological .....             | 1. Older brother imprisoned for theft.   |
|                                | 2. Parents were rigid, uncompromising; may have been war victims in Poland; status unknown.  |
|                                | 3. Wife and two children, though patient boasts of recent engagements with local woman friend.   |
| Occupational—Educational ....  | 1. Concluded 6th grade, capable of completing 8th grade requirements.  |
|                                | 2. Window washing prior to service; truck driver in service.   |
|                                | 3. 50 hours training as power machine operator in tailoring trade—terminated because of condition of left leg.   |
|                                | 4. Superior performance in leathercraft at X Va Hospital but attended irregularly.   |
|                                | 5. Vocational analysis suggests tooling, metal lathing, engraving as representative job objectives providing hand condition permits.   |

Present Status

DISCUSSION

A 29-year-old veteran with bilateral leg amputation, secondary to Buerger's disease—service-connected. Following amputation, 1948, patient attempted to protect lacerated skin edges by holding knee flexed. This resulted in muscle contraction, causing flexion deformity of left stump at knee. Complains now of pain and swelling in right hand and wrist. Casual encounter suggests that veteran accepts disability cheerfully and is free from anxiety. He is jovial and boisterous, but this is defensive front. Moodiness, outbursts of temper, petulance, surliness, and arrogantly demanding behavior are predicted reflecting highly disturbing anxiety. Other indirect evidences to be found in scattered, unsustained working habits, acceptance of only superficial and immediate goals, and unwillingness to face facts about himself or to obligate himself to responsibilities.

Veteran attempts to hide his present insecurity feelings, fear, and hostility. This pattern of pre-tense has grown from fear of retribution by authority. The following have contributed to this pattern:

1. Rigid, uncompromising parents who would not tolerate defiance.
2. Became bitter social and community outcast when brother was imprisoned for theft; veteran dared not express his feelings.
3. Successive amputations plus affliction of hand regarded by veteran as outrages inflicted on him though he was blameless. Fears that the same process undergone in his legs is being repeated in his hand. His fear and apprehension progress in direct accompaniment to suppressed rage against authoritarian bodies responsible. Regards self as akin to a monster—with monstrous impulses which only the fear of authority restrains. He feels obliged to conceal his real impulses, for the same forces which created "the monster" have the power both to punish and to heal.

Constructive versus destructive factors regarding rehabilitation are as follows:

<i>Destructive</i>	<i>Constructive</i>
Physical debilitation (legs, hand)....	Health otherwise good
Low education (5th grade).....	8th grade potential
Intellectual limitation in verbal, formal, scholastic sense.....	Superior performance ability with potential for objective type tasks requiring superior skills
No job specialty or job objective....	Same as above plus superior interests in mechanical, manipulative-type field
Excessive anxiety symptoms and discouragement .....	Youth permits considerable readjustment emotionally
Lack of motivation preeminent; \$250.00 compensation; plans for employment limited .....	Wife and two children to encourage responsibility and effort
Instability, irresponsibility, constriction of potential ability.....	3½ years with infantry and a clear record
Resentment of authority.....	High motivation to walk

### *Prognosis*

Deferred, pending more information about hand condition. Apprehension on patient's part over even further physical debilitation presents bleak outlook to him. This fear depresses motivation for any rehabilitation beyond the physical. Long-standing emotional problems and discouragement conducive to progressive instability. Potential for explosive, threatening, perhaps dangerous, behavior.

### *Medical Therapy*

#### ASSIGNMENT RECOMMENDATIONS

Diagnosis and treatment of hand with assurance that veteran's symptoms are not a part of Buerger's disease, and that all phases of physical restoration will be explored and carried out. Immediate recommendations are:

(a) Exploration of lump on wrist. If fluid is obtained, a part should be cultured and part should be oxalated without delay. A cell count should then be done, but using normal saline instead of acetic acid. (b) Complete blood chemistry including uric acid content. (c) Consultations with internist and orthopedic surgeon.

### *Physical Therapy*

(a) Whirlpool massage and exercise of both knees. (b) General relaxation exercises.

### *Corrective Therapy*

Quadriceps setting and general strengthening exercises.

### *Occupational Therapy*

Tonic and metric—both knees.

### *Educational Therapy*

Work toward 8th grade diploma with emphasis on arithmetic. No courses should be involved which are superfluous to practical objectives.

### *Manual Arts Therapy*

Exploratory research. Specific recommendations to await completion of diagnostic study of hand.

### *Psychological Medicine*

(a) Psychological sponsorship is indicated only at superficial level. The therapist should limit attention as much as possible to supportive type therapy and to superficial habit adaptation. Changes in this plan will emerge in discussion conferences between psychological sponsors and the control therapists, including chief psychiatrist and chief clinical psychologist.

(b) Direct and intensive psychotherapy is indicated if superficial therapy proves insufficient and breakdown threatens.

### *Social Service*

Contact regional office to

(a) Investigate the home situation and wife's attitude toward veteran;

(b) Educate her to meet problems arising relating to patient's handicaps, particularly emotional.



Vocational Rehabilitation and Education

- (a) Vocational retesting, if necessary, when condition of hand has been conclusively ascertained.
- (b) Initiate action for on-the-job training under PI 16 when patient is cleared by Rehabilitation Board.

RECOMMENDATIONS FOR ALL THERAPISTS

- (a) Keep his established goals in front of him, advising him of progress toward them. Purpose: to provide encouragement and reassurance.
- (b) Assist him in adapting himself and to accept his handicap.
- (c) Adopt attitude of tolerance and fairness, but firmness and impartiality. Purpose: to promote sense of responsibility, in that question of rehabilitation rests ultimately with patient.
- (d) Foster competitive spirit with other amputees. Purpose: to promote drive and motivation.
- (e) Be on alert for emotional outbursts, threatening or destructive behavior. Notify his psychological sponsor or Department of Psychological Medicine at once.

.....  
Chief of Clinical Psychology

.....  
Chief of Neuropsychiatry

.....  
Chief of Physical Medicine

DISCUSSION BY BOARD

The following questions were asked and points emphasized in discussion:

Q. What is the dividing line in aggressiveness when direct psychotherapy should be started?

A. The psychological sponsor will keep in regular contact with you and can help you decide. He, in turn, will keep the neuropsychiatrist and chief clinical psychologist in close touch with the progress of the case so that help is available at all times. Generally speaking, any threat of physical aggression should be reported for consideration.

Q. How should we react when he demonstrates aggressiveness or pettiness?

A. Treat him firmly but keep own feelings under control. Lay out his work matter-of-factly with the unspoken but well-understood expectancy that it will be done. Give recognition to his constructive achievements, remembering that such achievements are substitutes for aggression, and a means of getting recognition. Give it to him gladly. The more recognition he gets of this type, the less he will feel the need to show destructive aggression.

Final Disposition of Case.—Dr. D. moved, and the motion was seconded by Dr. W., that the above recommendations be accepted. The motion was carried.

Approved.....  
Chief Medical Officer.

IN CONCLUSION

The term "rehabilitation" is a working definition of the psychosomatic concept. In order to carry out this Gestalt type of thinking, the emphasis of therapy must be changed from aggregation to integration of diagnostic, planning, and treatment services.

The Fort Thomas staff is coordinating and integrating its functions as quickly and efficiently as possible to effect this change. Its interpretation of the *psychosomatic concept in working clothes* is presented in this paper through its three-step process: 1. The integrated diagnostic study; 2. Controlled planning; 3. Therapy and follow-through.

HALLUCINATION AND IMAGERY INDUCED BY MESCALINE<sup>1</sup>

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*St. Louis, Mo.*

The hallucinations induced by mescaline have been studied repeatedly in the hope of gaining greater knowledge of the mechanism of hallucinosis, particularly in schizophrenia.

The schizophrenic state is most commonly marked by auditory hallucinations, whereas visual changes predominate in mescaline intoxication. These include a subjective intensification of color perception, the appearance of colored haloes, and definite hallucinations, sometimes highly elaborated. Marshall (1) regarded the repetition of the same forms in different subjects, the more frequent occurrence of hallucinations in dim light and the precipitation of hallucinations by pressure on the eyeball as evidence of the primacy of retrolental structures, particularly the choriocapillary circulation; he believed that a "state of mind given to fantasy" was also important.

Knauer and Maloney (2) claimed to find an increased sensibility to color in mescaline intoxication, but their report is not sufficiently detailed to permit analysis or repetition.

That other than peripheral neural factors are involved is suggested by the failure of hallucinations to move when the visual fixation point is changed (3). Maclay and Guttman (3) overcame the difficulty of relying exclusively on verbal reports of visual experiences by utilizing artists as their subjects. Drawings made of the hallucinations either at the time of their occurrence or after recovery were studied, leading to the conclusion, "All of the pictures presented

show features well known in the physiologic process of seeing or in pathologic conditions due to organic lesions of the visual apparatus." In some instances physiological factors appeared to predominate, whereas other hallucinations represented fantasy formation with virtually no reference to the physiological mechanisms of seeing.

Stockings (4) believed that the visual and auditory psychic centers were affected by the drug. He said that mescaline intoxication could be described as a state in which there was a turning from reality and an eruption of the subconscious, so that the content of the hallucinations would be determined by the past experiences of the individual.

Knauer and Maloney (2) reported that, during mescaline intoxication, visual images such as were present in normal reverie might occur, and could be distinguished from the hallucinations. Zucker is quoted by Stockings as having found that, while schizophrenic patients could distinguish mescaline-induced hallucinations from their usual hallucinations, patients with toxic psychoses did not recognize such induced hallucinations as abnormal. Stockings pointed out that this might be due to the difference in sensory modality between the hallucinations of schizophrenia and mescaline.

The effects of mescaline on more complex psychic operations are repeatedly reported. These include the production of elation, suspicion, and dejection. Stockings has characterized the various changes in thinking and feeling as regressive. Bromberg and Tranter (5) felt that the anxiety experienced during peyote intoxication was due to the fact that the ego was threatened by the altered perception of the subject's own body. Wertham and Bleuler (6) suggested that constitutional factors accounted for the paranoid attitude frequently manifested during mescaline intoxication. This opinion was based on their observation that, of a number of subjects, only one showed significant

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This investigation was supported in part by funds of the Frank Phillips Foundation and the Simon Grant for Research.

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change in personality structure as revealed by comparing Rorschach tests performed before and during intoxication. In this one subject, the test record in the toxic state supposedly gave the truer picture of the subject's real personality. Guttman(7) also administered the Rorschach before and during mescaline intoxication, using a split test. While he did not report on the personality as a whole, he did state that not only was there an increase in the total number of responses, but also a relative as well as an absolute increase in the number of movement and color responses.

The relation of imagery to hallucinations has been investigated by several groups of workers with results that are not entirely consistent. Earlier work is best summarized by Cohen(8) and Klüver(9). Schilder and Kanner(10), asking normal subjects to imagine various objects and situations, produced experiences as varied and uncontrollable as the hallucinations of mescaline intoxication.

In addition to the rather vivid *imagery* described by Schilder, the same word is also used to refer to the feeling that, if one were to have a sensory image, it would take place in a specified modality. A test intended to measure such imagery was described by Griffiths, and was used with slight modification by Cohen(8), who found that schizophrenics tended to give fewer responses of an auditory or visual nature than did normal subjects. The tendency toward decreased imagery in these modalities was particularly strong when the patient had auditory or visual hallucinations, the corresponding imagery score usually being reduced.

Seitz and Molholm(11), using the same test, found that the presence of auditory hallucinations in schizophrenia and the recent presence of such hallucinations in patients recovered from alcoholic hallucinosis was associated with a decreased number of auditory imagery responses. Schizophrenic subjects without auditory hallucinations did not differ significantly in imagery test performance from normal control subjects.

In a series reported by Roman and Landis(12) the estimate of the schizophrenic subject as to strength of imagery was used.

The two subjects who had both auditory and visual hallucinations claimed to have strong imagery in the auditory and visual modalities. All of the 18 subjects with only auditory hallucinations claimed to have strong visual imagery and all but two of these also claimed strong auditory imagery. All patients stated that hallucinations were different from imagery quantitatively as well as qualitatively. Some of the quotations given in support of this distinction suggest that the patients were speaking not of their experiences but of their opinions about the origin of the hallucinations ("Voices come from telepathy but images do not").

The problem raised by Cohen as to whether, in schizophrenia, altered imagery produces or results from hallucinations, or whether neither of these changes is primary to the other has not been solved. In a subsequent publication(13) Cohen and Snyder cast doubt on the technique on which Cohen's earlier conclusions had been based, claiming that schizophrenic deterioration made it difficult to obtain reliable results with a test such as he had described.

In our investigation we have compared the imagery of our subjects during mescaline intoxication with their imagery on a previous occasion in an attempt to learn whether deficient imagery is an effect of hallucinations or a factor predisposing to them.

#### EXPERIMENTAL

Mescaline sulfate in doses of 0.2-0.4 gm. was given orally to 1 neurotic and 5 schizophrenic subjects in the morning while they were in a fasting state. All subjects were selected as being sufficiently cooperative and coherent to give valid responses to the imagery test. None had been known to experience visual hallucinations. Tests of color perception using a flicker fusion machine and quantitative determination of the excretion of mescaline were carried out on the experimental subjects as reported in another paper(14).

In the imagery test the subject was asked to state in which sensory modality he imagined each of the 130 stimulus situations

utilized by Cohen(8), Cohen and Snyder (13), Seitz and Molholm(11).<sup>3</sup>

This test was given within 2 days of the time of administration of the drug and was repeated 30 to 180 minutes after ingestion of drug. In order to estimate possible changes due to practice or to other conditions of the experiment, the imagery test was administered to 7 normal controls on 2 occasions, the second being after they were tested for color perception as the experimental subjects had been.

The behavior of the patients was observed and they were questioned concerning their subjective experiences during the period of toxicity and on the next day.

A brief description of the 6 experimental subjects and of their reactions follows:

*Subject A* was a 26-year-old woman weighing 139 pounds. Hebephrenic schizophrenia of 8 months' duration was manifested by neglect of personal appearance, silliness, auditory hallucinations, and inconstant poorly systematized, widely ramified delusions about being able to project her thoughts, etc. When given 200 mgm of mescaline sulfate, she showed no change in behavior, thought content, or affect. Direct questioning failed to reveal any evidence of actual hallucinations, or of distortions of form, color, or vividness.

*Subject C* was a 122-pound male of 31 years who had suffered from paranoid schizophrenia for 5 years. He heard voices saying "you will be killed" and suffered from corresponding delusions, but no longer showed adequate emotional responses to these beliefs and experiences. He showed no change in visual experiences except on one occasion 4 hours after receiving 300 milligrams when he stated that a pinpoint of white light in the screen was red. The patient talked more freely than usual about his religious delusions while in the darkroom, but

was not otherwise different than when observed on the ward before the test.

*Subject S* This 43-year-old, 95-pound female with simple schizophrenia of at least 10 years standing showed flattening of affect, lack of drive, and a childishness in her speech as well as in her devotion to pet cats to the exclusion of human society. Aside from ill-defined complaints that some change had occurred in her viscera several years ago, nothing that could be called hallucinatory or delusional was ever noted. After drinking 300 milligrams of mescaline sulfate, she noted a few flashes of light of undetermined color. She was nauseated for 4 hours, and had 3 emeses in succession at 2 hours. She observed numbness of the extremities during the same period, and was certain that this was not the same as the discomfort usually attendant upon nausea.

*Subject J* was a 26-year-old male hebephrenic schizophrenic weighing 155 pounds who had been ill for at least a year, and had been given shock treatment several months earlier without improvement. He had been disturbed by auditory hallucinations throughout his illness, and admitted indistinct olfactory and gustatory unusual experiences. Patient was very apathetic, his speech was self-contradictory but relevant and coherent. He was given 400 milligrams of mescaline sulfate. At 30 minutes, he observed that his limbs felt heavy. At 1 hour, while in a dim room, he commented on the heightened contrast between light and shadow, and described a light spot on the wall as a hole. At 2½ hours, he said that the surroundings did not seem real, and that his mind was sluggish. When looking in the flicker fusion machine, he described a variety of colors even when only white light was present and complained that the light never stopped flickering, even when it was constant. He complained of a persistent flicker for as long as 11 hours after medication. He was hesitant and uncertain in manipulating the flicker machine, frequently commenting on his inadequacy.

*Subject P* was a 35-year-old man, weighing 138 pounds, who had suffered from paranoid schizo-

<sup>3</sup> Some of the stimulus phrases and responses given by subject P are here given to illustrate the test-process. R1 = response before mescaline, R2 = response under influence of mescaline.

Stimulus No. 1—Opening an umbrella:

R1—See an umbrella there.....Scored: visual.  
R2—Touch it ..... tactile.

Stimulus No. 2—Features of the members of your family:

R1—Seeing them .....Scored: visual.  
R2—See ..... visual.

Stimulus No. 3—Ring of bells:

R1—You see. You can picture a bell in your mind.....Scored: visual.  
R2—Hear it ..... auditory.

Stimulus No. 91—Stooping to tie a shoestring:

R1—Touching .....Scored: tactile.  
R2—I picture a box of shoe polish..... visual.

Stimulus No. 117—A pocket knife:

R1—Touch it .....Scored: tactile.  
R2—I'm in such bad shape this morning I can't imagine.....Not scored.

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phrenia for some 18 months. He was uncertain of his masculinity, and believed others regarded him as a homosexual. He had frequent auditory hallucinations of his brother's voice, and often complained of dragging sensations in his abdomen. These he believed due to the action of a nerve in his penis. Forty-five minutes after being given 400 milligrams of mescaline sulfate, he complained that the light of the fusion machine looked like an eyeball. At 1 hour, the light of the machine was reported to have disappeared momentarily. He spoke often of his ideas of reference, and seemed at the point of tears. Between 2 and 3 hours he was very suspicious, and insisted that someone was lurking in the hall outside the room. He saw a white beam of light coming around the curtain of the dark room as red. On the day after the experiment, he confided to a nurse that he had noted terrifying changes of the features of the examiner at a time corresponding to his period of suspicion. He also said that he had seen "strange things" which he would not describe.

*Subject I* was a 20-year-old male, weighing 206 pounds, whose neurosis was manifested by fear of crowds, and by voyeurism. This man had some experience with optical instruments and was aware of the existence of afterimages and of the greater acuity of the peripheral field to dim light. Dizziness and gastric discomfort were reported 20 minutes after ingestion of 400 mgm of mescaline sulfate. Vision seemed to flicker at 30 minutes, lines on the wall began to writhe, and the contrast between light and shadow was enhanced. At 55 minutes, he noted sensations of cold and tingling. At this time, he saw 2 spots of light which were hallucinatory. At 65 minutes, a white spot of light appeared and took form of a human eye. Numbness and heaviness of the body persisted and visual undulation, lateral as well as forward and back, was noted continuously. At 2 hours this undulation took on a new expression, his knuckles appearing to swell and shrink. Two hours and 10 minutes after taking mescaline, he hallucinated black and white spots, and shapeless flashes of orange, yellow, and purple light.

## RESULTS

*Systemic Effects.*—The usual changes of nausea, pupillary dilatation, flushing, subjective weakness, subjective feeling of unusual well-being alternating with malaise were observed in the majority of subjects. Nausea was the most common complaint.

*Visual Phenomena.*—The observers experienced and the neurotic subject reported such normal occurrences as afterimages, and the greater sensitivity of the peripheral visual field to dim light. The schizophrenic subjects neither volunteered nor admitted that they were aware of such matters. Whether this difference was primarily one of experi-

encing or of reporting we do not know, although the latter seems more likely. This difference between the neurotic and psychotic subjects may bear on the fact that the neurotic reported a greater variety of hallucinatory phenomena than did the schizophrenic subjects. The hallucinations included increased vividness of actually existing colors, apparent alteration in facial expression, undulation of surfaces and lines, waxing and waning in size, flashes, flickering, and formed objects. Dim and wavering light favored the development of hallucinations. The duplication of figures reported by other experimenters did not occur in our series.

*General Psychological Effects.*—The 3 subjects who had virtually no change in visual experience showed little other apparent change. Those who developed hallucinations also felt anxiety. The neurotic subject did not appear to be disturbed by his experiences at the time, but it was later learned that on leaving the hospital he gave up drinking for fear that alcohol might induce delirium tremens, although he was not a heavy drinker. This appears to be a reflection of the anxiety which he later felt on looking back on his hallucinatory episode, and also illustrates the way in which he utilized the experience in the service of his neurosis, making it a basis for denial of pleasurable activity. A delay in reporting was observed in the schizophrenic patient whose hallucinations ranked after those of the neurotic individual. At the time of the experiment he was obviously ill at ease, reluctant to stay in the darkened room. He became suspicious that someone was lurking in the hall while he was in the lighter room for the imagery test. However, he did not admit any hallucinations until the next day, when he explained that they had been related to his obvious fear. Just as the paranoid schizophrenic became more suspicious, the hebephrenic boy became more uncertain, self-effacing, and hesitant.

*Imagery.*—Since this study is concerned chiefly with the visual modality, the scores for visual imagery only will be discussed. All the patients given mescaline showed a decrease in the number of visual responses. Five of the 7 control subjects who were not

given mescaline showed an increase; one did not change, while another gave a decrease. The data are summarized in Table 1. Statistical analysis showed that the mean decrease in the treated group was statistically reliable, having a  $P$  value between 0.05 and 0.02. In order to determine whether the individual subjects showed significant variation in this respect, the interaction was calculated, and a  $P$  value of over 0.99 obtained, indicating that no significant difference between the various treated patients could be brought out by this type of analysis. Control subjects showed a mean rise of 5 responses, which was statistically reliable.

*Relation of the Various Experimental Variables.*—The dose, per cent excreted, original visual imagery, change in visual imagery, visual disturbance (hallucinations), and the corrected change in color thresholds

system. As the work of Schilder has shown, the intact nonpsychotic human subject is capable of experiencing visual phenomena qualitatively similar to those induced by mescaline. The phenomena described by Schilder show individual differences and are not fully under the control of consciousness though they may be voluntarily induced. The mescaline hallucinations are not intentionally conjured up by the subject. It seems likely that there are several phases to the production of hallucinations. The first is that in which the individual becomes aware of experiences that are usually disregarded. The second is the failure to recognize the true origin of the unusual experience. In addition, there occur further elaborations of the hallucinations, depending on the particular mental constellation of the individual subject.

TABLE 1  
ANALYSIS OF VISUAL IMAGERY SCORES

	<i>N</i>	Initial score	Second score	Mean change	S.D. mean change	Significance ratio
Mescaline subjects .....	5	31.6	23.6 *	— 8	1.8	5.7
Control subjects .....	7	25.7	30.7	+ 5	1.4	

\* After mescaline ingestion.

were ranked separately, and correlations were made by the rank order method. The results of such a procedure must be regarded as suggestive rather than conclusive because of the small group and the difficulty in ranking some of the items.

Original imagery correlated  $-0.70$  with the degree of visual disturbance; decrease in imagery after drug correlated only  $+0.30$  with visual disturbance, while visual imagery after drug correlated  $-0.90$  with visual disturbance.

Decrease in imagery correlated  $+0.50$  with size of dose,  $+0.40$  with per cent of drug excreted, and  $-0.70$  with change for threshold for emerald green.

Visual disturbance, which correlated only  $+0.30$  with change in imagery, correlated  $+0.84$  with dose. It also correlated highly with threshold for lighthouse red and Nile green.

#### DISCUSSION

The process of hallucinatory formation is dependent on the operations of the nervous

Thus, the neurotic patient noted alteration in the appearance of his fingers, and was able to recognize this as a result of the drug intoxication. Later he used this experience as a reason for giving up alcohol. The paranoid subject who saw alterations in the faces of those about him found these changes hideous and threatening; he incorporated them in his persecutory system.

It is necessary to state that imagery is an overworked term having several meanings. There are afterimages, explained in terms of adaptation and fatigue of the visual system. Eidetic imagery is somewhat similar to after-image, but occurs too long after the original experience to be explained in the same way. With regard to the test here described, there is no reason for concluding that the opinion of a person as to the way in which he imagines something necessarily indicates the way in which he does imagine. However, the test does constitute a measurement of verbal behavior in response to definite stimuli.

The results show that the subjects who

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developed hallucinations were the ones with lower original imagery scores. This suggests very strongly that a low imagery score predisposes to hallucinations. Whether the low score actually indicates weak imagery we do not know. When hallucinations occur, there is a further drop in imagery score, in proportion to the vividness of the hallucination. One possible explanation of the fall in imagery is that the subject may inhibit the response, "I see it," for some time after he has hallucinated because of the unpleasant affective tone now associated with "seeing things." This explanation is inadequate to explain why imagery is so low in those subjects who have not yet hallucinated, but who will do so with the aid of mescaline. One may speculate that the low initial score represents a repression of verbal activity associated with a given type of sensation, and that there is therefore a greater pressure of repressed material waiting to burst out in the form of hallucinations when mescaline weakens the barriers of consciousness.

#### CONCLUSION

Mescaline produces altered visual experiences of several types, whose vividness and degree of distortion is proportionate to the size of the dose. There are no sharp boundaries dividing abnormal sensibility, illusions, and hallucinations. Subjects who gave fewer responses of the type "I see it" when asked to imagine situations were more likely to hallucinate than other patients. Visual responses declined still further after administration of mescaline in a degree more closely related to the amount of drug given than to the vividness of hallucinatory alterations, even in those experimental subjects who reported virtually no alteration in actual vision. The fall in reported visual imagery was not found in control subjects.

#### ACKNOWLEDGMENT

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## USE OF SOMNOFORM AS AN AID IN NARCOANALYSIS AND NARCOHYPNOSIS<sup>1</sup>

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The utilization of various types of medications as adjuncts to analysis and hypnosis has rapidly expanded in the last decade. Numerous authors have amply summarized the historical and developmental literature, rightly stressing the work of Lindemann(1) as a pioneer in the field and Horsley(2) as the originator of therapeutic applications. World War II brought a great expansion in use beginning with Sargant and Slater in 1940(3), followed by the work of Froelich and myself in the summer of 1942 with amytal and pentothal in England. Grinker and Spiegel began late in 1942 their work of repeating already established British data and from here on the use of these popularly accepted and undoubtedly overemphasized intravenous medications is widely known. Palmer(4), in 1942, added a new drug, ether, and this technique was introduced following Palmer by myself in the American Army in England in the spring of 1943. These three techniques, intravenous amytal and pentothal and inhalation ether, were found of considerable value and were employed extensively in the 312th Station Hospital and the 130th General Hospital during the period of my direction of the treatment centers of these organizations. Nitrous oxide, employed first by Rogerson(5), was also studied.

During the work with the 312th Station Hospital and the 130th General Hospital and particularly during the Belgium Bulge ample opportunity for research was available and more than 1,000 cases of pentothal medication were studied together with some 500 ether cases and nearly 200 cases utilizing sodium amytal. Only about 40 patients were studied with nitrous oxide, owing to difficulties in its administration. As a result of observations on these cases, certain gen-

eral interpretations can be evolved which have completely borne out the independent work of Sargant.

Our general conclusions are that inhalation anesthetics are easier of administration from a technical point of view since they do not require venipuncture, a relatively harmless procedure but one which seems terrifying to some patients. On the other hand, inhalation drugs are equally undesirable to certain patients who for one reason or another fear asphyxia. This is particularly true of ether as compared to nitrous oxide. We can easily form, therefore, two general types of drugs predicated on the mode of administration.

In the intravenous group we have a second subdivision: that is, drugs which can be continued over a long period of time and drugs which in a relatively short interval induce sleep. Pentothal is the ideal example of the first type and sodium amytal of the second.

The use of pentothal has certainly been adequately presented in the literature and has been demonstrated to be superior to its predecessor, Evipan. It is of value from both a narcoanalytic and a narcohypnotic point of view and possesses as well an established pharmacological background. Employed in psychiatric technique where the patient is not permitted to lose consciousness it seems to be without noxious hazard. Pentothal seems to be, therefore, specifically of value where a patient requires a long-time probing session or where it is desirable to pass from the hypnotic period into consciousness at the end of the session. This is most useful in the treatment of gross hysterical phenomena or in the treatment of amnesia. Fabing(6) has shown the use of coramine during pentothal treatment of amnesias to be particularly valuable in bringing the patient back rapidly to full consciousness in situations where this is important.

Sodium amytal is most useful in acute traumatic anxiety reactions where it is desirable to release a large amount of emotion

<sup>1</sup> Read at the 105th annual meeting of The American Psychiatric Association, Montreal, Quebec, May 23-27, 1949.

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and follow by a period of sleep induced by the drug. Cases seen during the war, for example, so severely shattered psychologically as to resemble Parkinson's syndrome did extremely well with sodium amytal. The patient was given the drug intravenously to a point of relaxation following which abreaction was attempted, after which the patient was put to sleep during which process considerable suggestion was directed toward symptom amelioration on awakening.

It has also been our experience that certain cases that do not yield to pentothal may with sodium amytal achieve a greater loosening up with a consequently greater gain in information extracted. A very valuable maneuver in this connection consists in the previous administration of scopolamine, 1/300 grain, repeated two or three times intramuscularly over a period of an hour and a half just before the use of the amytal. Recently Sargent(7) has suggested the use of methedrin following pentothal or amytal which results in a constant flow of talk and may fire off an acute emotional reaction during which repressed memories pour forth in abundance.

Other drugs, of course, such as intravenous nembutal or phenobarbital, can be used but in our experience to date the two main drugs utilized for their specific reactive purposes seem adequate.

As we turn to the inhalant drugs, our experience with nitrous oxide, while limited, indicates that it possesses certain advantages over ether. It does not have the unpleasant smell and according to the technique of Rogerson utilizing a dental administration outfit can be handled directly by the patient himself. It is, therefore, of considerable value in an office situation. Its major drawback, aside from nausea, common to both, lies in the need for the heavy storage cylinder which is frequently hard to handle, especially if various mixtures with oxygen are employed. This problem is not insurmountable, of course, and if nitrous oxide were as useful as pentothal it would probably be the drug of choice. Unfortunately, however, its action is extremely fleeting and it tends to produce more excitement and hyperactivity in the patient which in many instances brings about a termination of the interview. Its value,

therefore, seems primarily limited to those instances where a short transitory hypnotic period is desirable and where the search for suppressed material is not necessarily deep.

Ether, while simple to administer by the ordinary drop method, possesses these undesirable qualities in an even greater degree. As a matter of fact, it is most useful in acute cases, particularly traumatic amnesias. For instance, during the major phases of the German break-through in the Ardennes, practically all amnesias and hysterias were treated in this manner. These cases were all fresh, for the most part being out of combat only a few moments. Consequently, brief probing would clear up the amnesia and was usually accompanied by an emotional outburst. Brief suggestion would easily clear superficial hysterical symptomatology. It is my impression, therefore, that ether is of most value in severe traumatic reactions secondary to profound emotional stress, particularly where time is an important factor.

In using the drug with civilian cases, ether is of secondary value to amytal or pentothal because of the excitement which it produces. According to our observations which parallel those of Sargent, however, it would seem that some cases of chronic anxiety do very well following excited outbursts whether or not the abreaction touches any basic repressed problem. In other words, it would seem that, if by the use of pentothal or amytal one cannot uncover the basic problem, simply firing off an emotional reaction through ether will to some degree relieve the free-floating anxiety. This technique can be achieved, as for example in veterans, by simply getting them to vent a number of their basic irritations about the Army—irritations which in some instances may be etiologically important but in many others merely represent symptoms of the underlying personality disorder.

It can be seen, then, that all of these drugs have their assets and their drawbacks and, more important, have specific areas for their maximal function. From our experience we would conclude that an ideal drug for these purposes would be preferably an inhalant, easy to administer, which does not produce undue excitement or nausea and

vomiting and which could be continued for a fair period of time without untoward effect.

Recent experiments with Somnoform in 38 cases indicate that it may be a drug approaching this ideal. Somnoform was invented by Rousseau of Bordeaux according to information received from the Stratford-Cookson Company(8) who manufacture it. It was introduced to the Dental School at Bordeaux by George Rolland and has been utilized in the United States for the past 35 years. Because it has been primarily used in dentistry, however, adequate pharmacological studies have never been carried out, but it has apparently been used safely in more than two million cases and to date no fatalities have been reported(9, 10). Recently it has been adopted by a number of medical men and our experiments indicate that it has apparently no major hazards when used as a psychiatric adjunct.

Somnoform is provided in 5-cc glass ampules which are treated to keep out actinic rays. Its original formula was ethyl chloride 60%, methyl chloride 35%, and ethyl bromide 5%. This formula was early found to be unsatisfactory and various changes were made, different formulæ being tested, until the present formula, ethyl chloride 83%, methyl chloride 16%, and ethyl bromide 1% was achieved. It has been in use about 25 years.

The ethyl chloride component represents the "allegedly hazardous" part, since many anesthetists have considerable aversion to this agent. In its present mixture, which cannot be compared to ethyl chloride alone, and used only as a hypnotic it would seem to have safety factors certainly equivalent to any of the other drugs so employed by psychiatrists. Ethyl chloride has a boiling point of  $12^{\circ}$  C. and, while not explosive, naturally creates pressure when temperatures are increased above this level. If kept reasonably cool Somnoform presents no danger. If exposed to high temperatures a tube may break, in which event the ampule simply cracks and the Somnoform escapes. This volatilization should not be confused with potential explosive hazard. It is, of course, inflammable but in ordinary psychiatric practice this introduces no special problem.

Methyl chloride has many of these characteristics and a boiling point of  $-21^{\circ}$  C. It is not explosive, however, and does not burn as readily. Ethyl bromide boils at  $40^{\circ}$  C. and is inflammable but not explosive. Its addition to the mixture prolongs the anesthetic action.

The administration of Somnoform is certainly simple. An ampule is introduced into the specially built Stratford-Cookson surgical inhaler, which consists of a metal face piece having a rubber margin, a metal framework consisting of several cylinders joined together, and a collapsible rubber bag. When the ampule is introduced, a small lever permits breakage of the tip, liquid is deposited on a gauze net, and gas generation begins immediately. A lever is provided to regulate the proportion of air and Somnoform as desired and the apparatus can be held by the operator or by the patient. The gas is reasonably pleasant—smelling primarily as ethyl chloride—and after a few inhalations with air the vent is shut off and induction begins. It is important in anxiety states to utilize a technique providing a large amount of air at first as this desensitizes nasal membranes, allays fear, and prevents coughing. When the air vent is closed, induction will occur in 3 to 4 breaths and we have found it more useful to administer a mixture of about  $\frac{3}{4}$  Somnoform and  $\frac{1}{4}$  air which provides a slower inductive rate. The apparatus is designed to preserve the Somnoform for a period up to 5 or 10 minutes, and even with considerable breathing an ampule will yield a functional hypnotic level for about 5 minutes.

If prolonged periods are desired, it is extremely simple to substitute ampules and in this way hypnotic levels have been carried for a half hour. As with any such agent the usual precautions for anesthetic administration should naturally be observed although special care is not actually essential.

Clinical reports in the literature indicate that the only physiological reactions noted are transitory tachycardia and a transitory blood pressure rise. Occasional flushing occurs and breathing may become slightly more rapid during the early phases. These are confirmed in our series. Nausea has been reported but has not been observed in any of our cases, and acute excitement, struggling,

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or panic reactions are only rarely reported and have never been observed personally. The agent is remarkably prompt in action and deep anesthesia can be actually induced in 1 to 1½ minutes. This rapidity of action is probably the only problem from a psychiatric point of view, since unless reasonable care is taken the patient may reach a deeper level than desired. It is easy in this case, however, to simply lift the light apparatus from the face following which rapid recovery will occur.

The apparatus also can be used along the lines suggested by Rogerson for nitrous oxide; that is, it can be handled directly by the patient and if an overdose is administered, subsequent relaxation produces an automatic removal of the apparatus when the supporting hand collapses.

In our experience Somnoform has been found to be equally of value in narcoanalysis and narcohypnosis. With amnesias recovery of memories is achieved fully as rapidly as with ether and, to a considerable degree, more rapidly than with pentothal. Abreaction can be produced as with any drug of this type in a much simpler fashion. Hypnotic levels are easily obtained and the entire apparatus and technique being shiny and suggestive certainly influence the patient toward a suitable hypnotic status. It must be remembered that the odor of the gas is not familiar and there is no question of being anesthetized, a problem which frequently comes up with the use of ether. Aftereffects so far as have been determined have been essentially nil as compared with the headaches, nausea, and feelings of dizziness following ether. Some of these findings can best be demonstrated by brief case presentations.

**CASE 1.**—An 18-year-old white female entered the hospital with a complaint of a sudden amnesiac reaction toward her family. She had been seen by a local physician who referred her to the hospital after having become hysterical following a failure to recognize her mother or father, claiming that while she remembered who she was she could not recall whether or not they were actually her parents. This, of course, represents a specific parental denial and obviously the etiology lies deep in the personality development of the patient. In view of her acute anxiety, however, it was felt that removal of the symptom would permit more rapid psychotherapy. The situation was briefly discussed

following which she was told that through the use of a drug which she would breathe her mind would be relaxed and she would be able to remember in detail all the experiences of her past. No suggestions or clues were given as to her relationships, but it was emphasized that as a result of the treatment she would be able to determine whether or not the individuals who claimed to be her father and mother actually were related to her. She was given a small amount of Somnoform and, after she had reached a hypnotic level, was asked if she remembered her parents. She stated that she did and began to describe them and as she came to full consciousness suddenly cried that these were the people who claimed her and the complete amnesiac episode evaporated. Obviously the underlying personality problems were still present and were treated later by long-term psychotherapy.

**CASE 2.**—This patient was a war neurosis who presented considerable anxiety and demonstrated a small insular amnesia focused about the death of a buddy. His amnesiac period began during a bombing episode in the Pacific, and once the bombing started all that he could remember was the fact that he was in a foxhole or trench and that later he heard his buddy had been burned to death. He felt there was some further relationship but "everything was just blank." He was given some very brief preliminary instructions and, as always, the suggestive approach indicating that memory would return with the drug was used. Somnoform was then given and only one ampule was necessary. The patient rapidly achieved a hypnotic level and was then led back by verbal description to the period of bombing. He suddenly abreacted in a typical fashion similar to reactions of pentothal or ether. He demonstrated acute fear and began to cry to his buddy whom he apparently saw covered with incendiary material, burning like a torch. He ran toward the buddy and then began to cry that he could not go further and apparently turned and ran, hiding himself in the trench and leaving his buddy to be consumed by the flames. With Somnoform, it is comparatively easy at this point to bring the patient to rapid consciousness. This patient, following this technique, retained complete memory for the episode and later was able to describe it in detail although with each repetition he manifested considerable emotional reaction concerning the guilt which had possessed him as a result of his failure to assist his buddy. Naturally this problem had to be worked out from this point psychotherapeutically as is usual following any type of abreaction produced by any of the various techniques.

It is obvious from the above cases that the use of Somnoform does not contribute a new technique to psychiatry and does not substitute for psychotherapy. It presents a combination of drugs rapidly and easily administered by inhalation, easily controlled, and presenting few of the hazards or psy-



chological difficulties of previously utilized agents. About the only area in which it does not supersede existing techniques is in comparison to sodium amytal where for therapeutic reasons it is specifically desirable to induce sleep at the end of the analytic or hypnotic session. As a substitute for pentothal, nitrous oxide, or ether, it would seem to be more adaptable.

To date not much is known concerning the basic chemical and physiological action of Somnoform in the body. At this point I suppose, in accordance with the writing habits of my predecessors, I should introduce a theoretical discussion concerning the cortical site of function and outline a basic theory explaining the dynamic action of this particular agent. Previous writers have profoundly explained the mechanisms of various drugs inducing hypnotic states with subsequent analysis and abreaction in accordance with Pavlovian theory, or Freudian theory, or theory dependent upon their own personal belief. Sargant<sup>(11)</sup> has masterfully compared Wesley's results with emotional abreactions attributable to God, Grinker's results attributable to Freud, and his own results understandable on a Pavlovian basis.

In addition to these assorted theories, some authors more brilliant or perhaps more imaginative than others have been able to postulate the actual site of action of their particular drug in the cortex. In my observations on Somnoform, I can only state that as a clinical method for the reasons above indicated it is easy to use in office

practice and apparently achieves the same results as other drugs more extensively studied. I can further state that I have little knowledge as to the site of action and even less factual knowledge as to any theory accounting for its results. As a matter of fact, we have little knowledge of its pharmacological or physiological action. All that can be truthfully said at present is that clinically it represents a most useful adjunct in the field of narcoanalytic and narcohypnotic techniques. Certainly further investigation is indicated.

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## CYTOCHROME C: EFFECTS OF INTRAVENOUS ADMINISTRATION IN PRESENILE, SENILE, AND ARTERIOSCLEROTIC CEREBRAL STATES

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Recent advances in biochemistry have made possible promising approaches to the problem of the chemistry of the nervous system in health and disease(1, 3). The tremendous implications of biochemical and biophysical methods of research in cellular activity carried on by Caspersson in Stockholm in regard to protein metabolism and protein synthesis were the subject of the Salmon Memorial Lectures at the New York Academy of Medicine in 1948.

The techniques for the study of enzyme systems have also reached a point where they can be applied to the enzyme systems of the brain and other nervous tissue. The results of such studies made of the cytochromes led us to select a group of cases in the pre-

morbid disturbances in the enzyme systems, fluid imbalances, and alterations in electrolyte concentrations resulting from insufficiency or nonutilization.

### THEORETICAL CONSIDERATIONS

Cytochrome is an enzyme, a "heme" compound that is widely distributed in body tissues(6). It plays an important part in the oxidation system in the tissues. It undergoes alternate oxidation and reduction, but unlike hemoglobin it is not autoxidizable or but very slightly so. In order to take up oxygen it requires the aid of tissue oxidase; in order to undergo reduction it requires the presence of dehydrogenases. These acti-

TABLE 1

Metabolite or Substrate	$-2H$ dehydrogenase	pyridine nucleotides .....
flavoproteins .....	succinate-fumurate cycle .....	
cytochromes .....	cytochrome oxidase .....	oxygen

senile and senile group, with or without cerebral arteriosclerosis, for observation before, during, and after intravenous administration of a commercially available preparation of Cytochrome C. These cases had been admitted to the psychiatric service of the University of Virginia Hospital because of psychopathological manifestations. It was felt that the cellular and tissue changes associated with these states were particularly suitable for study of enzyme effects(4, 5).

This study must be considered as a biochemical experiment based on observations of 17 cases of senile and cerebral arteriosclerotic states in whom a respiratory tissue enzyme, the oxygen transferring Cytochrome C, appeared indicated because of possible

vate the hydrogen of organic molecules in the tissue cells which become hydrogen donors. Cytochrome acts as a hydrogen acceptor. In this way cytochrome, it is suggested, serves as an intermediary in the transference of oxygen liberated from hemoglobin, to the oxidizable materials in the tissue cells(7).

In the presence of suitable enzyme, certain hydrogen atoms in the metabolites of cells are made active and removed and the hydrogen acceptor can be passed on to one or more "carriers" before it is finally oxidized. The activation of hydrogen and oxygen is possible only if both the hydrogen of the metabolite and the oxygen are activated. Before the hydrogen can be transferred to the oxygen it must be "carried" by one or more substances (see Tables 1 and 2).

<sup>1</sup> Read at the 105th annual meeting of The American Psychiatric Association, Montreal, Quebec, May 23-27, 1949.

TABLE 2

Oxygen
Cytochrome Oxidase
Cytochrome A
Cytochrome C
Cytochrome B
Succinate-fumorate
Flavoprotein
Pyridine nucleotide
Substrate (containing hydrogen)

Hydrogen is removed from metabolite (or substrate, or, as it may also be called, food-stuff) and this hydrogen is carried by a series of "carriers" until it ultimately combines with oxygen to form water.

Such a "carrier" is cytochrome. It is an iron-pyrrole compound of the heme type, combined with a protein that is not globin. It is a mixture of three hemochromogens, which are referred to as a, b, and c. These are distinct compounds though only one of these, Cytochrome C, has been isolated.

The cytochrome studies have been sufficiently documented by many workers. Outstanding, however, are some that carry nervous system application. Efforts have been made by some investigators to study the functional conditions in the tissues of the nervous system. One of the most successful of these showed a correlation between cytochrome-cytochrome oxidase activity and differentiation in the embryonic nervous system. Howe and Mellors devised a method by which they could determine the cytochrome oxidase activity in normal and regenerating neurones of the thalamus and anterior horn cells of the spinal cord. They observed a reduction of cytochrome oxidase activity from 22%-23% in anterior horn cells during the regeneration following injury and of about 35% in the thalamic structures. Cytochrome C injected into rats intravenously, intraperitoneally, and intramuscularly increases Cytochrome C content in the brain. In dogs it appears to increase the arteriovenous oxygen. In the presence of cyanides, carbon monoxide, or sulphides that poison the oxidase, oxidation of cytochrome is inhibited. On the other hand, anesthetics that depress the action of dehydrogenases prevent

its reduction. In either case the link in the chain of oxygen usage is broken. Elson found that deficiency in B vitamins lowered the Cytochrome C concentration in liver tissue. Other evidence suggests that the energy required for lipide phosphorylation, a very important nervous system element, is provided by oxidations through the cytochrome systems. Cytochrome C has been shown with oxidized adrenalin and ascorbic acid to cause considerable increase of oxygen uptake and of rate of disappearance of ascorbic acid (8-11, 18).

The vital part, therefore, in the metabolism of cells played by the cytochromes seems to be quite widespread and is just beginning to be properly appreciated although still not too well understood. The experimental work already done on Cytochrome C suggests that respiratory enzymes such as Cytochrome C might be employed in the problems of tissue anoxia, acute and chronic, and in many cellular needs, especially during attempt at regeneration of nerve cells. These conditions would seem to be outstanding in the presenile and senile brain, with or without arteriosclerosis where ganglion cells undergo the typical changes of involutional atrophy and degeneration with interactions of parenchyma and glia, which are subject to much variation. Roizin and others report variable peroxidase and indophenol reaction in the presenile brain and in most instances it was reduced, diminished, or absent in the ganglion cells. Where these changes have not reached the irreversible stage we feel Cytochrome C intravenously administered has encouraging response particularly where the individual does not have longstanding neurotic or psychotic manifestations.

Cytochrome C as prepared by Wyeth is a clear, stabile, sterile solution containing 50 mgm. of the purified enzyme in a 5 cc. volume of saline. The enzyme is extracted from horse and beef heart tissues by a process that yields a pyrogen-free solution. Acute and chronic toxicity studies in mice have revealed no pathological tissue changes and blood pressure experiments in dogs gave no perceptible effect on circulation or respiration.

Normally there is no Cytochrome C present in the circulating blood, the blood stream

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presumably acts as a reservoir from which organs take up additional Cytochrome C as needed and to which organs release Cytochrome C when no longer needed. It is reported that 50 mgm. injected intravenously will gradually disappear from the blood stream in 24-48 hours (man and dog). Doses of 350 mgm injected intravenously will result in gradually diminishing levels over a period of 5 to 6 days. It is conceivable that if further studies continue to show Cytochrome C to be nontoxic a single large injection may be used to serve as a supply for several days or longer. We used the daily administration method.

#### PROCEDURE AND CLINICAL OBSERVATIONS DURING AND AFTER ADMINISTRATION OF CYTOCHROME C

In a series of 17 patients in a biochemical experiment, the schedule was as follows: After clinical evaluation of the case as suitable for trial on Cytochrome C, which for our purposes was to include the senile, presenile, arteriosclerotic, and involutional states, an initial electroencephalogram and psychometric test were given. To begin the course of injections, we did an intradermal skin test for possible sensitivity. In no cases were there any signs of sensitivity. After a negative skin test, 1 cc. of Cytochrome C was given intravenously the same day. On the following day 2 cc. were given intravenously, on the third 3 cc., and thereafter 5 cc. daily for a total of 14 days. In the middle of the course or about the end of the first week a second EEG was taken while the injection was being made. At the end of the course, a final EEG and another psychometric were given. *In the second group of 2 cases, the treatment was speeded up.* After the initial skin test and trial injection of 1 cc., the patient was given 5 cc. intravenously twice on the second day, morning and evening. After that 10 cc. were given twice daily until a total of fifteen 5-cc. ampules were used. The EEGs were obtained before, during, and after the course and the psychometrics before and after as in the first series. The daily dosage in the first group was 50 mgm. per day and in the second group was 200 mgm. per day.

In no case was there any untoward reaction to the injections. One or two patients who were rather neurotic and suggestible did mention slight feeling of giddiness or lightheadedness immediately after the injection. Several others noted transient feelings of exhilaration.

Of the 17 cases treated to date, it was *not* felt that all were equally suited. Based on the theory that the Cytochrome C enzyme might improve brain function in those cases in which impairment of function is presumably due to poor tissue respiration, we attempted to select those cases fitting into the syndromes of the presenile or early senile and early arteriosclerotic changes. However, a number of cases were accepted that were known to have large "functional" factors in their illness, or in whom psychological conflicts were thought to be prominent, such as the involutional reactions and various neuroses. In 2 cases it was felt likely that irreversible changes had taken place in brain cells because of advanced long-standing arteriosclerosis and severe residuals of cerebral vascular accidents.

Of the 17 cases observed, 11 were thought to show clinical improvement and 6 to show none during and after administration of Cytochrome C injection. Of the 11 improved cases, 4 seemed to improve only during the course of treatment with no sustained tangible benefits. Seven showed some degree of sustained improved function. Over a period of time varying from 4 weeks to 9 months, follow-up reports tend to indicate that these individuals are getting along satisfactorily outside the hospital. Two cases seemed to show marked immediate improvement after starting injections and this was sustained for several months with gradual lapse into pretreatment state. No attempt was made to keep patients on Cytochrome C beyond the trial period, such as on a bi-weekly or weekly dose except in one case, where continued improvement was noted on this program. She is still on this plan of procedure.

All the cases showing sustained and fairly definite improvement fell into the category of typical early senile and arteriosclerotic types with memory defects, tendency to

disorientation, confusion, irritability, etc. (Table 3).

Those cases showing unsustained improvement fell largely into the neurotic and functional psychotic classes. The effect of suggestion could not of course be accurately evaluated but was thought to play a part in these cases. Of the 6 "functional" cases, 1 later responded well to electroshock and 2 improved markedly with psychotherapy. Two of the "organic" cases showing no improvement had suffered severe cerebral vascular accidents just prior to treatment and one of these died after prolonged coma. It was considered that these should be discarded from the series in evaluating results, but should be reported.

The ages of the patients in this series averaged 66+, ranging between 43 and 79, with the majority in the sixth and seventh decade.

utes following the injection. Hyperventilation periods were obtained on the patients before the Cytochrome C injection as well as the end of the Cytochrome C injection. A third EEG was obtained on the patient at the end of his Cytochrome C injection series.

The EEGs were obtained on a Grass 6-channel Model III machine, and silver disc electrodes with paste and collodion were employed. A standard monopolar 10-lead technique was used. Approximately 2½ minutes or 120 deep breaths were the standard hyperventilation procedure. In each case the average dominant frequency was obtained from the control record at rest, during hyperventilation, 15 to 25 seconds after hyperventilation and 60 to 70 seconds after hyperventilation ceased. These average dominant frequencies were then compared with the corresponding dominant frequencies found

TABLE 3

Clinical diagnosis	No. cases	Sustained improvement	Transient improvement	No improvement
Functional disorders (involutional, manic-depressive, and neurotic).....	6	0	4	2
Organic disorders (senile and arteriosclerotic) .....	9	7	0	2
Cerebral accidents .....	2	0	0	2

#### ELECTROENCEPHALOGRAPHIC DATA ON PATIENTS RECEIVING CYTOCHROME C INJECTIONS

Proger and Dekaneas noted that electroencephalographic changes produced by anoxia can be largely prevented by Cytochrome C and that impairment of visual discrimination, which is one of the earliest measurable functions in cerebral anoxia, could be overcome within 5 minutes by injections of 60 mgm. of Cytochrome C(12).

Six of our patients who received injections with Cytochrome C were studied electroencephalographically. Each patient was given an EEG prior to his Cytochrome C injection for control purposes. A second EEG was obtained during the middle of the experiment, approximately a week after first injections. During this EEG the patient was given a Cytochrome C injection and the tracing was taken for approximately 30 min-

utes in the record taken in the middle of the Cytochrome C injections and at the end of the Cytochrome C injections. The only changes noted in the comparison were the following:

1. In the control record there was a change with hyperventilation, the brain waves becoming slightly faster or slightly slower during hyperventilation and gradually returning to that of the resting state.

2. In the second recording there was less change with hyperventilation than there had been in the control record.

3. In the final EEG record there was either no change at all during and following the hyperventilation period or else there was only a slight change, the frequencies increasing by only one or less than one per second.

The tentative conclusion that this suggests is that the Cytochrome C or the procedure of intravenous injection has a stabilizing effect on the brain waves, particularly during and following hyperventilation. The

Cytochrome C injection on the brain waves

PSYCHOTIC CASES  
Control

Eleven cases of senile dementia were included in the study. The course of the disease was variable. Some patients had been in the hospital for several years, while others had been in the hospital for a few months. The patients were selected on the basis of their clinical picture and the results of the EEG examination. The patients were divided into two groups: those who had been in the hospital for more than six months and those who had been in the hospital for less than six months. The results of the EEG examination were compared with the clinical picture and the results of the EEG examination.

The role of cytochrome C in the treatment of senile dementia is not yet clear. It is known that cytochrome C is a powerful antioxidant and that it can protect the brain from the effects of anoxia. It is also known that cytochrome C can improve the function of the brain in various conditions of disease. The results of the EEG examination in the present study suggest that cytochrome C may have a stabilizing effect on the brain waves, particularly during and following hyperventilation. This effect may be due to the antioxidant properties of cytochrome C or to its ability to improve the function of the brain.



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Cytochrome C, however, did not alter the brain waves to any noticeable extent.

#### PSYCHOLOGICAL STUDIES BEFORE AND AT CONCLUSION OF CYTOCHROME C ADMINISTRATION

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Eleven patients who were given Cytochrome C were tested on the Wechsler-Bellevue Intelligence Scale, Form I, before the course of therapy was begun, and the Wechsler-Bellevue, Form II, after the therapy was completed. In no case was there a significant difference in the actual scores earned on the 2 forms of the test, but in every case the report of the second examination noted qualitative improvement, such as increased speed of response, increased alertness, decreased confusion, greater ability to comply with instructions, greater ability to verbalize, and more relaxed behavior. In some cases there was a consistent tendency for the subtest scores on Form II to be higher than on Form I, but as noted above the over-all difference was never great enough to be considered statistically significant(13).

#### SUMMARY AND CONCLUSION

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Theoretically and experimentally the vital rôle played in cellular metabolism by the cytochromes as respiratory tissue enzymes is recognized and appreciated(14). This apparently also applies to tissue activity in the nervous system, particularly during growth, differentiation, and regeneration following injury. Cytochrome C, a commercially available preparation, was selected for clinical trial in cases of presenile and senile states with or without evidence for nervous system arteriosclerosis. We fully recognize that there are other equally important enzyme systems involved in cellular metabolism, notably riboflavin or flavoproteins and pyridine nucleotides. The latter has the important nicotinic acid amide component serving as a reversible hydrogen acceptor and is indispensable for the action of a great many dehydrogenases. However, catalytic action of Cytochrome C is still a link in part of the oxidation going on through these systems. The relation of cellular oxidations to lipid phosphorylation is also thought to be through oxidations by the cytochrome sys-

tem(11). Cytochrome C, therefore, seemed to be a good choice for trial(15, 16).

Clinical improvement was noted in a majority of cases observed in regard to memory, orientation, irritability, interest, confusion, and behavior. Only slight changes were observed in the electroencephalographic recordings and these changes may be insignificant. Psychometric examination showed qualitative improvement in keeping with clinical improvement and a trend toward higher scores.

The changes noted in these patients during the trial period are quite in contrast to the results obtained in the problem of treatment of the senile states for the previous 3 years on the psychiatric service. During that period 27 cases were diagnosed as senile reactions. Of these, 6 were improved and, of these 6 cases, 4 were treated with electroshock. The remaining 21 cases were referred to state institutions, domiciliaries, nursing homes, or sent home as unimproved. These cases were given the routine supplementary vitamin therapy, symptomatic care, special diets, and routine activity programs which were also part of the program for the cases reported in this series.

Total duration of mental illness, as judged by reviewing the literature, in the senile psychotic state tends to be from 1 to 3 years, generally less than 2 years, and when improvement takes place it most generally does so within 2 or 3 months time. Because of the heavier and increasing burden to mental hospitals, any aid to hasten possible improvement and the care of the aged seems justifiable when psychological and physical factors combine to incapacitate the individual.

We wish merely to report these studies as observations, making no claims beyond the theoretical about specific action or changes produced by this enzyme. We feel encouraged, though, by the clinical changes noted during the short observation period. The biochemists can give us little help in interpreting these observations beyond theoretical speculation but neither can they tell us what happens to cellular metabolic processes in nervous tissue as a result of electroshock or insulin therapy. We, nevertheless, use such therapy because it works. The pharmacologists express themselves freely

that the rôle of cytochrome in cellular respiration is well established but they are very skeptical that injected cytochrome can be utilized as such by the body tissues. However, practically no work has been supplied by either the pharmacologists, the experimental biologists, or pathologists that would indicate Cytochrome C to be of any utility in the therapy of pathological tissue states such as those in which we are interested.

More promising and encouraging are apparent results from Cytochrome C noted by us in our trial of it in acute toxic inflammatory reactions of the nervous system, about which we hope to report separately at a later date.

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## GERMAN PSYCHIATRY DURING THE WAR

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The structure of German military psychiatry during the war inevitably reflected the conditions and working plan of German civilian psychiatry with all its peculiarities. The field is organized on a strictly authoritarian basis. It is necessary, for example, for the young doctor in Germany who hopes to become a leader in psychiatry to resign himself to the limitations of an academic career. He must expect to spend long years as a subordinate assistant before he attains to the distinction of being an *Oberarzt* or the assistant chief of a clinic. During this time individuality and independence of thought are not encouraged. He is most successful who most completely absorbs and reflects the opinions and methods of his chiefs.

The same respect for acceptance of authority which was seen within the civilian system was, as might have been expected, emphasized and intensified by military rank and discipline.

The structural organization of the psychiatric service within the armed forces is shown in the accompanying chart. In general the leaders from academic psychiatry were given high rank and became the leaders of military psychiatry very much in the same way as in the States.

The echelons having thus been set up with some of the old professors at the head, the older assistants in the intermediate positions, and the young assistants serving with troops, a system of official communication had then to be established with the direction of flow from above downwards.

Two media of communication were used primarily. These were the *Sammelberichte*, very similar to our technical bulletins and the *Richtlinien*, small bulletins of instructions on particular technical matters.

The *Sammelberichte* comprised reports of interesting cases, descriptions of trends, large numbers of particular kinds of cases being seen, new methods of treatment, instructions on diagnosis and treatment, and occasionally criticism of mistakes which had been made. The very usage in these publications was again an authoritarian rather

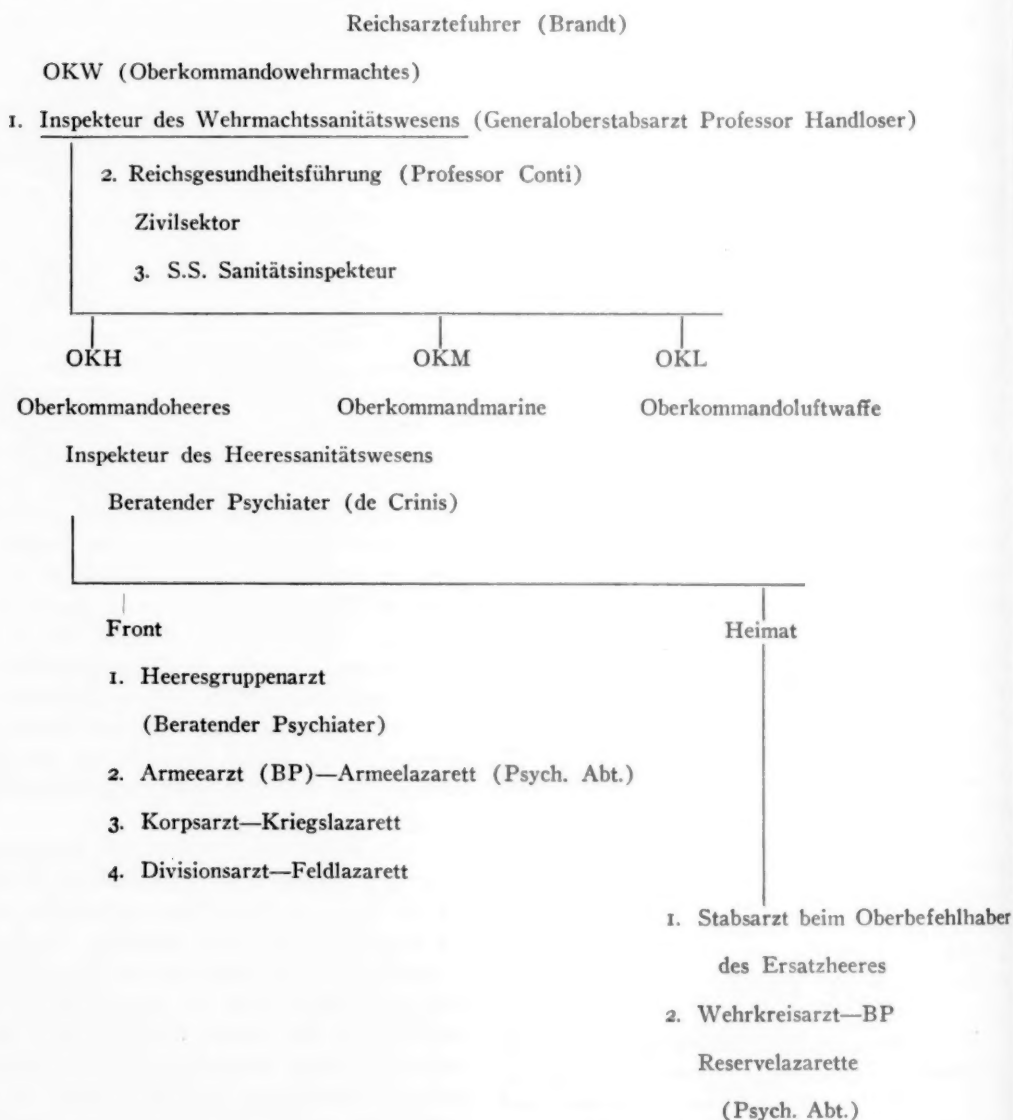
than an experimentally oriented one. The information which was put out, for example, was usually begun by "Professor De Crinis says" or "Professor Kretschmer reports." Seldom, if ever, was a series of cases statistically presented. Much more emphasis was placed on neurological and medical-legal classification and disposition than on psychotherapeutic treatment. The Germans had a fairly complicated system to classify degrees of ability to perform military service. Individual German soldiers seem to have felt that this method of classification was careless and brutal in the extreme. Their statements, of course, are always suspect because of the possibility of their having emotionalized, misunderstood, or frankly lied about the true situation. I have, however, heard from several individuals that two medical examinations were done on the soldier before he went to the front, one at the time of induction and one at the end of preliminary training. These individuals said that it was the custom to parade an entire battalion for this examination. The doctor appeared before them and asked any who had complaints to step out of ranks. If none did, all members of the battalion were considered able to do duty (*Dienstfähig*).

From the doctor's point of view, however, the business of classification of individuals seems to have been approached with considerable care and attention to detail. One of the major functions of German military psychiatry was to formulate written opinions on the status of soldiers (*Begutachten*). These documents were of the utmost importance in deciding whether or not individuals would be punished for violation of military discipline. Again, exactly as in the American system, the actual decision as to whether or not to punish a man lay always with the military court. The statement of a psychiatrist, however, seems in many cases to have ranked only slightly below divine revelation and was almost always followed. Psychiatry in the German Army was given much more latitude in the evaluation of legal re-

sponsibility than is possible under American military law.

Under ordinary circumstances a psychiatric patient was admitted first to the field hospital. It seems that no attempt whatever

able. This section was made up of 3 physicians with 30 to 100 beds at their disposal. Even in this echelon, however, only the most mechanical of care was given, and the main function, which was one of triage, divided



(BP indicates Consultant Psychiatrist in that echelon)

was made to treat these patients in forward areas. Almost all patients admitted with a psychiatric diagnosis to field hospitals were evacuated to corps and army hospitals without question. In the army hospital there was usually a psychiatric section, this being the first echelon in which such service was avail-

the patients into those who would recover spontaneously and be returned to the front, and those who must be returned to a psychiatric hospital in the homeland.

My only information about what actually went on in these psychiatric services is fragmentary. One gathers, however, that there

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was little or no understanding of psychodynamics and no attempt whatever at psychotherapy. The old mechanical methods, shock, baths, sedatives were used and wherever any therapeutic activity evidenced itself it tended to be of a strict, repressive kind.

In one such hospital patients with certain symptoms were classified as having "the war shakes" (*Kriegszitterer*). These patients were housed together and their only treatment consisted of castor oil given each day in a larger dose until the patient asked to go back to the front, at which time, regardless of his condition, the request was granted.

In another hospital galvanic electricity was used roughly in the same method, progressively increasing the dose until symptoms disappeared.

An example of the kind of treatment which was used together with the nature of material to be found in the official publication can be demonstrated by quoting a rather long excerpt from one of the *Sammelberichten*:

Attention is called to the results of Dr. Klaubert, in the military hospital at Rodewisch, using electro-suggestive treatment of psychogenic disturbances of bladder function (113 cases treated, particularly nocturnal enuresis and urinary retention). The particular method, and its results are cited by the author:

The patients are begun on treatment by evening of their day of admission, whenever that is possible. For the most part they are not awakened at night, do not use rubbersheets, and the feet of the beds are not elevated. They are told that they themselves are responsible for their bladders.

The treatment continues with verbal suggestion and galvano-faradization with 10 MA, increased in serious cases up to 60 MA.

The method of treatment aims at two goals:

1. The regulation of the depth of sleep.
2. The strengthening of the bladder-sphincter.

1. The regulation of the depth of sleep is attained through electrical treatment of the arms and legs with 10 MA, or in special cases with 20 MA. Either a very small dose of faradic current was applied,  $\frac{1}{2}$  to  $\frac{3}{4}$  of the galvanic dose, or the thing would be done exclusively with galvanic electricity. The patient was told, "The electricity has strong healing powers. It is able to stimulate circulation and metabolism; improve appetite and digestion, make sleep less deep and abnormal, lighter and more refreshing than it has hitherto been. Then you will be able to notice when the bladder feels full, and will awaken because of that feeling."

2. Finally, the flat electrode was placed over the lower spinal column, and brush or roller electrodes were touched to the region over the symphysis 5 or 6 times for very short times (fractions of a

second) with 40-60 MA current. This was done after having the patient in full expiration. The patient was then told, "The muscle which closes the bladder is strengthened by this treatment, so that it can completely close off the bladder, and so that when you wake up at night you are sure to make it to the toilet."

In 98% of the patients the bladder dysfunction is improved. The patients are then treated twice more in the next 2-4 days in the same way, to consolidate the improvement. In the first night after treatment they are usually particularly wakeful, waking 3-6 times, but in the following nights they wake up only 2-3 times and the emptying of the bladder then takes place normally. In case the first treatment is not successful, a somewhat more intensive treatment is given, and two additional treatments always bring success, in the course of a few days. Fluids are not restricted, but on the contrary, provocative tests are done by giving large amounts of tea and beer in the evening. In the case of urinary retention the bladder is percussed before the treatment and, if the bladder is thereby found to be full, the patient is encouraged to urinate immediately after the treatment. Also with urinary retention on psychogenic grounds prompt success is attained after the second or third treatment, even with those who have had to be catheterized 1-2 times daily. Catheters and urinals are taken and kept away at the first treatment.

In numerous cases patients stated before treatment that they could not be helped, since their father and sisters or various of their children were bed-wetters. The cases too were promptly cured.

Most cases remained 3-4 weeks in the hospital, to rule out relapse and particularly to prepare newcomers morally and physically, by means of sports and drill for return to duty. Relapses in cases of psychogenic bladder dysfunction have not been seen, while from the remaining 110 psychogenic dysfunctions treated, 8 were readmitted, of whom 2 were known malingerers.

With a current of 10-60 MA the patients need practically never to be held [*gehalten*] during the treatment.

Those patients who were considered seriously ill were transported back through the medical channels and eventually arrived in the larger civilian psychiatric hospitals. Most patients who got back this far never again did military duty. The disposition of patients from the large psychiatric hospital involved not only the ordinary factors of diagnosis and prognosis, but also had to be considered under the race purification laws. According to a law made effective on July 14, 1933 (National Law Book, vol. 1, page 520, changed later by the law of June 26, 1935, National Law Book, vol. 1, page 773, and the law of February 4, 1936, National Law Book, vol. 1, page 119) sterilization could be ordered and enforced on persons suffering

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from the following diseases: (1) congenital mental deficiency, (2) schizophrenia, (3) manic-depressive psychosis, (4) hereditary epilepsy, (5) Huntington's chorea, (6) hereditary blindness, (7) hereditary deafness, and (8) severe inherited physical malformation.

It was further possible to sterilize persons suffering from severe alcoholism. Legal courts were set up to adjudge and order the sterilization and certain clinics were authorized to perform the operation. It was expected that directors of psychiatric hospitals would report to the civil authorities those persons suffering from the above diseases. Since the members of the courts had high regard for the opinions of the hospital directors, under ordinary circumstances the original diagnosis was not questioned. This, of course, put tremendous power in the hands of the psychiatrists and I think it may be said to their credit that most of them were embarrassed and oppressed by that power.

There was even some organized resistance to this program of sterilization. I have been told that a certain Dr. Rittmeister headed a group of 40 doctors who agreed among themselves never to make any of the diagnoses listed above. Instead of them, they used euphemisms or code diagnoses referring for example to schizophrenia as "tendency to encephalitis." Dr. Rittmeister was a member of the 20th of July Resistance Group and was hanged for his part in the unsuccessful plot against Hitler's life.

In any case there are many persons in Germany today who were sterilized under this German law. I, myself, have seen several men with the small bilateral scars over both inguinal regions.

Going even farther in August 1943, a directive (*Bericht*) was issued from Hitler's headquarters (*Führerhauptquartier*) which directed that persons diagnosed as homosexual be put to death. It is said that this directive was prepared by the research section of the Goering institute in Berlin by a committee composed of De Crinis, Conti, and I. H. Schulz. I have not seen a copy of this directive, but have been told about it by a colleague of Dr. Haseloff, who was a member of the research section in the Institute. The language of this directive ordered euthanasia for homosexuals on the

grounds that all such persons suffered from congenital unworthiness (*Erbminderwertigkeit*).

In German psychiatry today the same main differences are found which existed during the war between American psychiatry and German psychiatry. Much emphasis continues to be put upon anatomy, pathology, and neurology. The work of Kretschmer has directed interest to bodily types (*Körperbau*). There is a good deal of activity in the field of the shock therapies. On the side of understanding dynamic psychology of the individual and treating psychiatric problems with psychotherapy there is very little activity. Psychotherapists in general are grouped together in their own organizations and are separated from hospitals and universities. It must be said, however, that this separation now seems to be decreasing.

In 1947 I had occasion to visit one of the better German psychiatric clinics. The assistant director of the clinic was kind enough to show me over the entire hospital. The hospital itself, in spite of the difficulties then inherent in the German economy, was in good order and the patients were well cared for. Food supplies had been supplemented from hospital gardens. Shock therapy was being administered and, in addition, a most excellent neurological laboratory was functioning with all of the usual apparatus, but also with much unusual or greatly refined apparatus. These methods of mechanical investigation were really striking in their complexity and practicability. Much impressed, I said to the professor as I was leaving the hospital, "What about psychotherapy here? Who does it and what methods do they follow?" He answered, with complete lack of interest, "I'm not quite sure, but I think one or two of my assistants are interested in psychotherapy."

In many cities of Germany to this day there are minor feuds going on between the professor of psychiatry in the university and the leader of the local organization for psychotherapy (psychoanalysis).

For practical purposes psychotherapy is represented in Germany by psychoanalysts although these adhere to various schools. In the American Zone of Occupation there are now psychoanalytic institutes active in Ber-

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lin, Munich, Stuttgart, and Heidelberg, and individual analysts with excellent reputations scattered about in various other places. These men and their science did not have an easy time of it during the war. Psychoanalysis was considered by the Nazis a "Jewish science" and was first looked down upon, afterwards interfered with, and finally forbidden.

Professor Müller-Braunschweig, the dean of the Berlin Institute, has given a description of the vicissitudes of that institute during the war. From the beginning of the Hitler régime there was noticed in the analytical movement a progressive loss of interest. The Jewish members who had begun to leave before Hitler came into power almost all disappeared by one route or another. The Jewish members who remained in Germany came to the conclusion, as a consequence of the growing anti-Semitic measures, that they could best serve the psychoanalytic association and protect German psychoanalysis by resigning from the association. This, of course, was not an easy decision to make. After some time, all psychotherapists were united into one national organization under the leadership of Professor M. R. Goering. The psychoanalysts, after much discussion, also joined this organization. In Berlin in May 1936 there was founded the German Institute for Psychological Research and Psychotherapy, under which title many strange bedfellows came together. Adherents to the school of Freud, Kunkel's Adlerian School, and members of the school of Jung at first had relative independence within the institute although this had progressively to be given up. It had been stated in the statute by which that institute was founded that all of the furniture and the library of the Berlin Psychoanalytic Institute should be placed at the disposal of the new institute as a loan. These things, incidentally, were destroyed later in the bombings.

At first in 1937 the same practices were followed of lectures, seminars, and teaching analyses, but these were limited more as time went on. First the old titles of the lectures were changed into tortuous new ones. The evening lectures, for example, were entitled "Conference Evenings for Casuism

and Theory" (*Referaten-Abende für Kasuistik und Theorie.*) Later, either Professor Goering or his wife attended all the evening sessions as censors to ensure, among other things, that not too purely psychoanalytic terminology was used.

It seems that Professor Goering was well intentioned and did what he could to protect the psychoanalysts but had also from time to time to give some thought to his own health.

In 1938 when Austria was occupied, Professor Müller-Braunschweig managed to get appointed to go to Vienna to take over the Psychoanalytic Institute and its library there, having the personal intention of bringing all those things to Berlin and protecting them until better times. Unfortunately, his attempts directed the particular attention of the government to the problem of psychoanalysis and its "Jewish origin." At this time also a letter that Professor Müller-Braunschweig had written to Anna Freud unfortunately fell into the hands of the security service (*Sicherheitsdienst*) of the Gestapo and was considered to bring into doubt the trustworthiness of its writer. He was immediately forbidden to take any further part in lectures or public teaching. Furthermore, all the commitments which the régime had made with the institute were cancelled and the Vienna Institute, its rooms, and its press were liquidated. Finally as the bombings became more and more severe, the Berlin Institute practically ceased to function although a few of its members continued private practice in various nooks and crannies in Berlin. Many of them fled the city before the occupying troops.

To summarize, the administrative structure of German military psychiatry paralleled rather closely the American. Civilian personnel were utilized for the most part in the military structure. Mechanical forms of treatment were available and psychotherapy was almost completely neglected. Sterilization laws and the euthanasia directive represented a radical departure from anything we knew. The wide division between organic and dynamic psychiatry which existed during the war continues to be reflected in the structure of German psychiatry at the present time, although it is decreasing.



## CORRESPONDENCE

### SURVEY OF SHOCK THERAPY PRACTICES

*Editor, AMERICAN JOURNAL OF PSYCHIATRY:*

SIR: Experienced users of the shock therapies will agree that Dr. Manfred Sakel made an important contribution to psychiatric practice by introducing insulin therapy. The Manfred Sakel Foundation recently published the findings of a survey on the current status of shock therapy practices in hospitals throughout the country. The Foreword states, "The outstanding disclosure of this present inquiry is the extraordinary neglect to provide adequate training programs in the only generally available treatment [presumably the Sakel method] that gives promise of hope to the schizophrenics." The Foundation has asked for comments on the report.

The outstanding disclosure of the report is the widespread confusion in thought on the subject among psychiatrists after more than a decade of experience with these therapies. Another remarkable finding is that 65% of the hospitals "using insulin shock rely on the Sakel technique." That a treatment empirically determined should survive so long in its introductory form is not too flattering for the practice of psychiatry. The numerous variables in the hosts and the disease processes make necessary thoughtful modifications of any new treatment; and that most effective for the greatest number of psychiatric patients is a combination of known methods discriminately applied. It would be surprising if Dr. Sakel has not introduced modifications to the method he introduced at the Harlem Valley State Hospital in 1936.

Hypoglycemic therapy is undoubtedly effective for the treatment of schizophrenics, especially those of recent development. Failure to obtain uniformly good results in different hospitals is not explainable entirely by the comparative "skills of the doctors." The men who trained under Dr. Sakel and returned to their respective hospitals to practice with close adherence to his "classical"

method have not always achieved the best results. The knowledge that insulin administered under careful supervision in large doses is readily controllable led to the discovery of effective modifications to the Sakel method. There was no reason for indefinite continuance of debatable rules and criteria prescribed by Dr. Sakel. The method could not remain static. There was no point, for instance, to teaching "the correct psychological moment" for terminating coma, the graduated approach to coma dosage, or the special technique in discontinuing a course of treatment. Even while the courses were in progress at the Harlem Valley Hospital, in another department or building of the institution subcoma dosage treatment was in use, with favorably comparable results. The concept of insulin therapy had to rise above a purely mechanistic basis; the units of insulin per dose and even the total amount of insulin for a course of treatment (sic) were reported from some hospitals as determining factors.

The report notes that some hospitals are still prejudiced against shock therapy. Although shock treatment has become popular with relatives of patients, some psychiatrists have not been able to overcome their own resistance to the term "shock." The writer pointed this out quite a few years ago in urging a physiologic or pharmacologic concept of the treatments. This is not the place to renew discussion of such a concept, but it may be pointed out that an induced hypoglycemic reaction has complex physiologic effects upon the patient and the physiologic status incident to the disease. Thus insulin therapy is unique in the field of pharmacology; dosage depends upon wide individual variations in sensitivity, reactions are unpredictable, and even these may be modified by special techniques. The significance of convulsions during hypoglycemia is still a debatable subject in some quarters.

The nature of the questions on which the report is based detracts from the validity and



informativeness of the findings. A general criticism of the questionnaire is its biased wording in favor of insulin therapy by the Sakel method. Discriminate use of this method should also presume the use of various modifications in combination or in sequence with convulsion therapy.

The wording of questions 11, 12, and 13 and the answers indicate widely prevalent misunderstandings about shock therapy. At this late day in experience with the various forms of treatment, exclusive of psychosurgery, clearer concepts should be in evidence. Is a convulsion comparable to coma as "shock to the maximum possible therapeutic degree"? What is the basis for equating the two unlike reactions in the patient? Dr. Sakel at first considered the incidence of a convulsion cause for immediate termination of the hypoglycemic reaction, regardless of the fact that convulsions generally occur early in coma or the precoma stage. Presently patients are often allowed to continue in hypoglycemia if they recover from the convulsion without interference and without untoward effects, as most of them do. Actually, patients inclined to excitement and thrashing about, in the precoma stage, after a convulsion go into a coma with much less excitement. Dr. Jones' criticism of question 12 is more valuable than the "real replies" in the tabulations. His suggestion "to throw out all replies to sections (a) and (b)

of this question as being of doubtful validity" could apply also to (c) without loss of any valuable information. All reference to "maximum" and "minimum" dosages disregards individual sensitivity, variations in sensitivity during a "course" of treatment, and makes no allowance for the most important factors, the physiological reaction and the therapeutic effect. The discriminative therapist is concerned with a preconceived desired reaction in each case, the type and depth of response to the induced hypoglycemic state. Question 13 ignores the possibility of merit in "modified" forms of insulin treatments. This is unjustified in the light of much experience. Modification of the Sakel method has broadened the use of insulin therapy for a variety of clinical conditions and provided adjustments as needed for various types of schizophrenics. Question 14 involves assumptions that are not supported by present-day knowledge. There is no basis for belief that a spontaneous convulsion during hypoglycemia differs from an induced convulsion by electricity or a convulsant drug. Can convulsions produced by electric current be "resembling insulin coma" or was this "a slip of the pen"? The report is valuable in pointing to the need for trained personnel to administer shock therapy by all approved methods.

S. J. TILLIM, M. D.,

Nevada Hospital for Mental Diseases.

## COMMENT

### EDITORIAL AFFAIRS

During the calendar year 1949 there appeared in our pages 118 original contributions. Of these, 66 were papers that had been presented at annual meetings of the Association; 52 were contributions not appearing on the annual program but submitted during the year to the editorial office. This statement answers a question that has sometimes arisen in the minds of prospective contributors: whether other than program papers are eligible for publication in the JOURNAL.

The total number of manuscripts that must be considered annually has been gradually increasing, as might be expected in view of the increasing number of workers in the field of psychiatry. During the year 1948, 93 nonprogram papers were received; in the year 1949 the number was 113. The greater number of papers accepted by the program committee in recent years has made it necessary to set up additional sections at the annual meeting, and since 1947 there have been four sections regularly throughout the week.

It has been possible to print more papers latterly, as the tendency has been to submit briefer manuscripts. We believe this tendency is to be encouraged, not only in the interest of space-saving but particularly as favoring clear and concise presentation and time saving on the part of the reader. It is generally necessary to give priority to the briefer communications.

With the growing two-way traffic between psychiatry and other disciplines, occasional papers from the social sciences, such as

sociology, psychology, anthropology, education, are welcome; likewise from the fields of psychiatric nursing, social work, and rehabilitation. The number of acceptances from these various fields must naturally be limited.

The complexion of the scientific material published in the JOURNAL changes somewhat from year to year, dependent upon the nature of the annual programs and submissions from other sources. Topics in clinical psychiatry, in its broadest sense, are regularly the most often dealt with. Somewhat over half the papers published during 1949 are in this broad field. There appears to be a definite tendency toward increased reporting of work in the strictly medical fields, including laboratory studies and physiological and surgical treatment measures as well as psychotherapy. There has also been a wholesome and overdue increase in attention to administrative psychiatry; and such special fields as industrial, forensic, and military psychiatry have not been neglected.

During the past three years there have been several changes in the editorial board occasioned by death or retirement of former members. We are very happy in the appointment of our newest member, Dr. Leo Kanner, whose pioneer work in child psychiatry and whose textbook in that subject have brought him world recognition. Dr. Kanner's appointment materially strengthens the editorial board; his acceptance in spite of his many other commitments and his willingness to assume a share of the editorial tasks are deeply appreciated.

### "THE CREEPING PARALYSIS OF DEPENDENCY"

The title of this Comment, which we borrow from the *New York State Journal of Medicine*, suggests a psychiatric subject. Believing the subjoined editorial, which appeared in the Dec. 15, 1949, issue of that *Journal* to be not only of social and economic but also of psychiatric interest, we sought and obtained the kind permission of the man-

aging editor, Dr. George W. Kosmak, to reprint it. It points up admirably and, we think, without caricature the sickly sentimentality that promotes the "welfare state," for which, beyond political expedience, it seems difficult to find argument.

The deadleveling process involved, weakening or abolishing all sense of personal re-

sponsibility in matters of health, and that *ignis fatuus* "security," making the citizenry at large wards and dependents of the paternal state, is so contrary to the healthy process of individual growth and maturation that it cannot be regarded as contributing to the mental health and robustness of an adult society.

This editorial, one of a series in the *New York State Journal of Medicine*, merits the attention of the social planners.

"Physicians are in a position to assess the subtle corruption of dependency; they have to contend with it in many cases of illness in which it is a factor—the dependency which demands 'security' as a sop for the vague fear that all is not well, that creeping paralysis of the will which aggravates sickness, prolongs recovery, provokes relapses, and drives the cost of sickness ever higher, the cost of living ever upward, makes the tax bill ever greater; the dependency which exhausts the coffers of private charity, overloads public assistance, permits private taxation to be levied, for example, on every ton of coal

mined to be paid by every coal-using citizen for the 'health and welfare' of an elite protectorate who *may* work one or two days a week *if permitted*. Surely, they must need a 'health and welfare' fund of huge proportions since their house is 'empty, swept, and garnished,' ready for occupancy by the seven devils: idleness, vainglory, pride, preferment, tyranny, hate, and fear.

"Within the labor movement, dependency grows constantly, witheringly as a result of the pursuit of the will-o'-the-wisp 'security.' In the larger field of national affairs, authority is proposing 'social security' on an ever more grandiose scale, apparently unmindful that 'security,' whether social or not, is preceded by debt, accompanied by dependency, and followed by destruction.

"Consider the current public debt, consider the current commitments of this nation to others, consider the proposed domestic legislation to increase 'security' and increase dependency, citizen-taxpayers! Shall we travel that road to its end? Who then can be secure, from what and for how long?"

## NEWS AND NOTES

**EASTERN PENNSYLVANIA PSYCHIATRIC INSTITUTE.**—Dr. Hilding W. Bengs, Commissioner of Mental Health for Pennsylvania, informs us that Governor James H. Duff is speeding the development of a new State Psychiatric Institute to be established in Philadelphia. The new Institute was authorized by the 1949 session of the state legislature, and funds are provided through the creation by the same assembly of a General State Authority, a bond-issuing agency for public construction.

By statute the Eastern Pennsylvania Psychiatric Institute will provide for an inpatient service of 250 adults and 50 children, with all the necessary facilities for study and research in mental and nervous disorders, as well as for training and teaching on both undergraduate and graduate levels. Separate outpatient departments for adults and children will be included. The Institute will also provide regular courses of study for state mental hospital personnel.

The State Department of Welfare is charged with the planning in consultation with a Board of Trustees and a Medical Advisory Board, membership of each having been drawn from the five medical schools in Philadelphia. A suitable site has been selected and the designated architects are drawing up the plans and specifications.

The proposed Institute in Philadelphia is expected to share the Commonwealth with the Western Psychiatric Institute and Clinic in Pittsburgh. The latter was opened in 1942 and was transferred by lease agreement on September 1, 1949 from the Department of Welfare to the University of Pittsburgh for operation. These two facilities will serve as pilot plants to the Commonwealth's mental institutions and will be the foci of psychiatric training and research in Pennsylvania.

**DR. V. V. ANDERSON HONORED.**—To commemorate Dr. V. V. Anderson's 25 years of service as founder and director of the Anderson School, and in recognition of his pioneering work in psychiatry, mental hygiene, and education, members of the staff

presented to him an oil portrait of himself by the well-known artist, Hans Peter Hansen, at a brief ceremony on December 15, 1949 at the School.

During its first quarter century, the physical plant of the school (including the Fox-hollow Division) has grown to 22 buildings, and the grounds now include 760 acres. The enrolment is currently 169 students; on the staff are 29 faculty members and 48 other employees.

In his presentation address, Headmaster Lewis H. Gage pointed out that Dr. Anderson had organized the first child guidance clinics in this country, and that it was their development, together with his experience as director of personnel at R. H. Macy's, that led Dr. Anderson to study the inadequacies that he saw in the training of young people. The establishment of a school that would meet educational requirements and also do the more important job of developing the whole personality was the result of these experiences.

**DR. WOLFSON DIRECTOR OF NEWARK STATE SCHOOL.**—On February 1, 1950, Dr. Isaac N. Wolfson became director of Newark State School, which is one of six New York state institutions for mental defectives, located in the village of Newark, Wayne County.

His appointment to the directorship of the School marks Dr. Wolfson's 19th year in state service, which he entered at Hudson River State Hospital, Poughkeepsie. He has been assistant director of Manhattan State Hospital on Ward's Island since 1943.

**DR. MCNEILL JOINS STAFF OF NATIONAL INSTITUTE OF MENTAL HEALTH.**—Harry V. McNeill, Ph. D., formerly area clinical psychologist, Veterans Administration, New York State, is now regional mental health consultant in clinical psychology, assigned to the Public Health Service Regional Offices in New York City and Boston.



**PSYCHOBIOLOGICAL THERAPY.**—Dr. Wendell Muncie will give a course on the techniques of psychobiological therapy at the Postgraduate Center for Psychotherapy, 218 E. 70th St., New York City, beginning May 26. There will be 10 sessions, Fridays 8:30 to 10 p.m., and Saturdays 10:00 to 12:00 noon.

The course, open only to qualified psychiatrists, will exemplify the psychobiological viewpoint of Adolf Meyer.

**AMERICAN PSYCHOSOMATIC SOCIETY.**—The seventh annual meeting will be held at Chalfonte-Haddon Hall, Atlantic City, N. J., on Saturday, April 29, 1950. Because of the proximity of the annual meetings of the American Psychiatric Association and the American Psychoanalytic Association, there will be only one day of scientific sessions instead of two. A registration fee of \$5 will be charged to nonmembers. For further information write to the Society office at 714 Madison Ave., New York 21.

**AMERICAN ELECTROENCEPHALOGRAPHIC SOCIETY.**—The third annual meeting of this Society will be held at the Hotel Claridge, Atlantic City, N. J., June 9-11, 1950. On Sunday June 11 there will be a symposium on clinical and electrical aspects of temporal lobe disorder, under the chairmanship of Dr. Gibbs. The annual dinner (informal) will be on Saturday evening June 10.

The chairman of the committee on arrangements is Dr. John A. Abbott, Massachusetts General Hospital, Boston 14. Hotel reservations may be secured by applying to Miss A. Taylor, Hotel Claridge, Atlantic City.

The American Society of Neuropathologists will hold a meeting at the Hotel Claridge on the afternoon of June 11.

The American Neurological Association will hold its annual meeting at the same place June 12-14.

**ASSOCIATION FOR PHYSICAL AND MENTAL REHABILITATION.**—The fourth annual convention of this Association will be held May 23-27, 1950, in Memphis, Tenn., at the Hotel Peabody. The program has been planned to attract physicians, therapists, and others engaged in the field of rehabilitation. For in-

formation, write to the convention chairman, Mr. Clement G. McNamara, Physical Medicine Rehabilitation Service, Kennedy VA Hospital, Memphis 15, Tenn.

**WASHINGTON (D. C.) PSYCHIATRIC SOCIETY.**—At the annual meeting on January 12, 1950, Dr. George S. Stevenson was guest speaker. His address concerned the scope of psychiatric interests beyond the confines of immediate work with emotionally disturbed people. Dr. A. M. Duval also addressed the Society, on its early history and the progress of psychiatry in the Washington, D. C., area.

Officers for the coming year are as follows: president, Dr. Robert T. Morse; president-elect, Dr. Norman Q. Brill; secretary, Dr. Henry P. Laughlin; treasurer, Dr. Douglas Noble. Drs. A. M. Duval, George N. Raines, and David McK. Rioch were named to the Council of the Society.

**MASSACHUSETTS PSYCHIATRIC SOCIETY.**—At the annual dinner meeting of this Society in Boston last autumn the following officers were elected for the year 1949-50: president, Dr. Marianna Taylor; vice-president, Dr. John T. Shea; secretary-treasurer, Dr. David Rothschild; councillors, Drs. Walter E. Barton and A. Warren Stearns.

**MCGILL UNIVERSITY, TRAINING IN PSYCHIATRY.**—The training facilities of the department of psychiatry of McGill University have been greatly expanded during the last year with the assistance of funds made available through the Dominion-Provincial health grants.

These facilities are designed to prepare men primarily to enter the field of general hospital, university, community, and outpatient psychiatry. Major emphasis is placed upon instruction in psychotherapy and psychosomatic medicine.

A few openings remain for the year commencing July 1, 1950. Applications should be made to the chairman of the department of psychiatry, McGill University, Montreal, Canada.

**PHILADELPHIA GENERAL HOSPITAL, RESIDENCY.**—This hospital offers an approved residency in a 350-bed psychiatric unit. Both

acute and chronic illnesses of all types are seen. The staff includes many nationally known neuropsychiatrists. The facilities of the hospital are used by several medical schools in the city for teaching.

Residents are appointed for 2 or 3 years and receive training in neurology and neuropathology depending on their needs and desires. The stipend is \$75 per month with complete maintenance.

For further information write to the Office of Medical Education, Philadelphia General Hospital, 34th St. and Curie Ave., Philadelphia 4, Pa.

**TRAINING IN CHILD GUIDANCE CLINIC PSYCHIATRY.**—The American Association of Psychiatric Clinics for Children announces the availability of specialized training in child guidance clinic psychiatry, in a number of its member clinics approved as training centers by the Association. This training begins at a third-year postgraduate level, with minimum prerequisites of graduation from medical school, a general or rotating internship, and a 2-year residency in psychiatry. Fellowship stipends are usually \$3,000 for the first year of training and \$3,600 for the second year.

For further information write to Dr. A. Z. Barhash, executive assistant, American Association of Psychiatric Clinics for Children, 1790 Broadway, New York 19, N. Y.

**WORKSHOPS IN RORSCHACH METHOD.**—Western Reserve University's department

of psychology will offer three workshops in the Rorschach method, during the month of June. The courses will be introductory (June 5 through 9), intermediate (June 12 through 16), and advanced (June 19 through 23). Instructor in the courses will be Marguerite R. Hertz, Ph.D., who is a Fellow of the Rorschach Institute and associate editor of the Rorschach Research Exchange. Graduate credit will be given for each course, and the fee for each is \$40. For information concerning hours, admission to membership in courses, etc., write to the secretary of the department of psychology, Western Reserve University, Cleveland 6, Ohio.

**EXAMINATIONS, AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY.**—The Board announces that during 1950 there will be two examinations: June 23 and 24 in San Francisco immediately preceding the A.M.A. convention, and in December in the East. Early application is desirable to allow time for clarification of credentials. Deadline for applications for the June examination is March 15; for December, September 1. The first 300 eligible applicants will be accepted and those remaining will have to be deferred until 1951.

**NOTICE TO DIPLOMATES, AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY.**—The Board requests that any diplomates who have changed location since certification send to the Secretary their correct address and diploma number immediately.

#### THE AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY, INC.

The following were certified at New York City, December 5, 6, 1949.

##### PSYCHIATRY

Abrahams, Joseph, St. Elizabeths Hosp., Washington 20, D. C.  
Aldendorff, Herbert, 320 W. 76th St., New York 23, N. Y.  
Allen, Arnold, Suite 782, Reibold Bldg., Dayton 2, Ohio.  
Beckman, Wallace G., VA Hosp., Palo Alto, Calif.  
Bell, John Peay, 206 E. Chestnut St., Louisville 2, Ky.  
Berchenko, Frank, 1148 Fifth Ave., New York 28, N. Y.  
Bever, Christopher T., St. Elizabeths Hosp., Washington 20, D. C.  
Bikales, Victor W., Winter VA Hosp., Topeka, Kans.  
Bing, James Frederick, 715 Park Ave., Baltimore 1, Md.  
Bjorklund, J. Harman, 111 N. 49th St., Philadelphia, Pa.  
Blaustein, Milton J., 9 E. 78th St., New York, N. Y.  
Bolin, Neatha V., VA Hosp., Waco, Tex.  
Borras, Joseph Cavitt, 105 Carroll Place, New Brunswick, N. J.  
Bourkard, Ernest R., 349 Plant Ave., Tampa 6, Fla.  
Bowers, Frank C., Baker VA Hosp., Martinsburg, W. Va.  
Brannon, Earl P., VA Hosp., Perry Point, Md.  
Buckley, Robert W., 2508 Auburn Ave., Cincinnati, Ohio.  
Cale, Edward E., Jr., 14 High St., Natick, Mass.

Carra, A. D., 175 Vernon Ave., Northport, N. Y.  
Carter, James D., Johns Hopkins Hosp., Baltimore 5, Md.  
Cattell, James P., 722 W. 168th St., New York 32, N. Y.  
Cleckley, James Jennings, 267 Calhoun St., Charleston, S. C.  
Clement, Stephen Merrell, 537 Delaware Ave., Buffalo 2, N. Y.  
Cohen, Harry Wallace, 518 S. 57th St., Philadelphia 43, Pa.  
Conrad, Stanley W., 1822 Spruce St., Philadelphia 3, Pa.  
Crain, Irving J., 50 E. 78th St., New York 21, N. Y.  
Cramer, Joseph Benjamin, 261 Alexander St., Rochester 7, N. Y.  
Cronick, Charles Herbert, Box 5, Howard, R. I.  
D'Amore, Arcangelo, 1917 Eye St., N.W., Washington 6, D. C.  
Donovan, Eugene T., Ypsilanti State Hosp., Ypsilanti, Mich.  
Drake, Frank R., Walter Reed Gen'l Hosp., Washington, D. C.  
Drell, Hyman J., 311 Ellsworth St., Rockford, Ill.  
Drooz, Richard B., 435 Linden Blvd., Brooklyn 3, N. Y.  
Eden, David, Prince Georges Co. Men. Health Clin., Univ. of Md. Campus, College Pk., Md.  
Evans, J. Lawrence, Jr., 254 Christie Heights St., Leonia, N. J.

Swing, John  
Falsely, Edw.  
Ferguson, J.  
Fine, Berna  
Finlayson, S.  
Center, S.  
Palmer, Ed  
Foster, The  
Friedland, J.  
Fryer, Juli  
Mass.  
Gilbert, Lou  
Gioscia, Ni  
N. Y.  
Jarman, D.  
Jarris, Wi  
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Jager, Jac  
Jeffries, B  
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## BOOK REVIEWS

THE REACH OF THE MIND. By J. B. Rhine. (New York: William Sloane Associates, Inc., 1947.)

This book is concerned with telepathy (awareness of another's thoughts without sensory aid), clairvoyance ("awareness of objects or objective events without the use of the senses"), precognition (prophecy), and psychokinesis (levitation or mental influence on the movement of inanimate matter), to which the author refers as "psi" or parapsychic—popularly known as "psychic"—capacities. Among the aborigines and the unsophisticated the reality of such phenomena is generally accepted; not so among intellectuals. This book is obviously written for the purpose of convincing the intellectuals that the aborigines and the unsophisticated are right after all.

The book comprises a rather heterogeneous combination of statistics and anecdotal material—of premonition of a son's death come true, of dishes inexplicably smashed, doorbells rung, stones hurled by invisible forces through doors or windows, furniture found in disarray in locked rooms, sleepers disturbed by their bedclothes being pulled off, the sudden splitting of a professor's inkwell, the unaccountable splitting of an old, well-seasoned table top, and a psychiatrist's knife inexplicably broken into 4 pieces. These dramatic events are recounted in association with, and are expected to lay the groundwork for, scientific investigations based on statistics on cards called before and after the actual drawing and statistics on dice influenced by will power. However, the statistics lose by juxtaposition with the anecdotal material.

The test material for telepathy, clairvoyance, and prophecy is a set of 25 cards consisting of 5 each of 5 symbols (star, circle, square, cross, 3 wavy lines). The probability by chance alone is thus that 5 out of 25 cards chosen at random will be called correctly. The general procedure for telepathy tests was to have the sender think of the card and concentrate on it while the receiver tried to identify it. In the clairvoyance tests the card was drawn without the experimenter knowing which it was. In the more carefully controlled experiments, but not in all of them, the two participants were in separate rooms in order to prevent the transmission of sensory cues from one to the other.

In the first series of tests, the subjects scored over 7 hits out of 25, or 2 above the chance level. Later, however, when safeguards and precautions were introduced—namely, independent duplicate records of responses taken, locked boxes, and opaque envelopes utilized—the scoring rate dropped to 5.2 as compared to the mean chance expectation of 5. The author believes this drop to have been due to the fact that these precautions took the spontaneity and the playful challenge that is stimulating to extrasensory perception (ESP) out of the test situation.

It is of particular interest that the results were the same when clairvoyance and telepathy were employed simultaneously as when either of them was utilized alone. This is a very important finding, although it does not support the author's thesis. He tries to fit this finding into his thesis by claiming that this fact proves their basic likeness, both being manifestations of ESP. It appears to the reviewer, however, that when two like forces, whether they be physical or nonphysical, if exerted simultaneously do not either add to or detract from each other, the conclusion is justified that at least one, if not both, equal zero.

Prophecy was also rather inaccurate, the mean score being between 5 and 6 hits per 25 calls (with the probability of hits by chance alone being still at 5).

The mental influence on dice thrown by hand, cup, or machine likewise did not come up to the dramatic accuracy of stones thrown through windows by invisible hands. With a mean chance for 5 hits for high dice (8 or above) per series of 12 double throws, the actual average obtained was 5.5 hits per series, that is, half a hit above chance. The author as well as the authorities in mathematics whom he quotes regarded these scores as statistically significant (on the basis of 446 hits above mean chance expectancy out of 900 runs or 10,800 throws) and as evidence in favor of the existence of psychokinesis, that is, purely mental influence on the movement of inanimate objects; but the scores are certainly not impressive, and Rhine himself later calls them "inconclusive" (p. 94).

The real point at issue seems to be whether or not a fifth to a half of a hit above chance expectation per 25 calls (for telepathy and clairvoyance) or 24 throws (for psychokinesis) is significant.

The author seems to be aware of the weakness of the over-all statistics in themselves and buttresses his theories with the argument that the initial scores were frequently much higher than chance and later invariably declined—in dice throwing, usually from the third throw on; in card calling, either by clairvoyance or telepathy, usually midway through the test procedure. This successive decline of test performance, which applies to the single test as well as to the ability of the test person during subsequent trials, is regarded by Rhine as characteristic of extrasensory perception as well as of psychokinetic ability. The weight of this argument, however, is somewhat reduced in view of a statement made by Rhine on page 35. The subjects who were not found to possess any ESP ability after the preliminary tests were not further used, while "most of the tests, however, were conducted with a selected group of subjects who, in their preliminary trials, showed the capacity to score in the general range of from 6 to 11 hits per 25." It appears on the basis of this statement



that the subjects had no opportunity other than to decline in order to revert to the average expected by chance, since out of any large group a certain number would be expected to score higher than chance initially.

Also in that part of the book dealing with experimental findings, the only material with a convincing ring is anecdotal. There is the delightful story of Lillian, a 9-year-old orphan:

"The experimenter promised a reward of fifty cents for a score of 25, not seriously thinking she would have to give it. Candy prizes were to be given for smaller scores. Lillian, a serious child, was resolved to get a perfect score and win the half-dollar. She gave enough thought to the matter to declare her intention to Miss Pegram (the experimenter) in a letter written after one of the sessions. At the next one, a few days later, when her turn came, she said, 'Don't say anything—I'm going to try something!' She turned her back on the experimenter and stood for a moment with her eyes closed. When she turned again and went through the test, her lips kept moving as if she was speaking to herself. When asked what she was saying, she replied, 'I was wishing all the time, that I would get twenty-five.' *She did!* It seems clear that in Lillian's case we have an example of an attitude built up to a high pitch centering in the winning of the reward. In her subsequent scoring Lillian averaged little above 'chance,' even under identical conditions of testing."

I do not know exactly what this story proves. Whether it means that the gods are kind to little orphan girls or whether it means that little orphan girls have guardian angels who can look through paper, or whether Dr. Rhine, the aborigines, and the unsophisticated are right I am not prepared to say.

Dr. Rhine feels that ESP and related psi functions are ephemeral, "erratic," "unstable," "unpredictable," subtle, "elusive," "shifty," and "baffling" phenomena. Believers do better than non-believers. "Expansive" people do better in clairvoyance tests than "compressive" people. Boredom and frustration affect these functions adversely (it is thus that Dr. Rhine explains the low scores made when the cards were placed in opaque envelopes), and they react favorably to "playful challenge."

Dr. Rhine feels that in their unpredictability and sensitiveness extrasensory perception and psychokinesis bear a similarity to artistic performance. It is therefore surprising to find him expressing in his concluding chapter the belief that souls surviving after death, which he refers to as incorporeal or discarnate personalities, could communicate with each other and the living world only by extrasensory means, telepathy and clairvoyance, and by psychokinesis, although he is not prepared as yet to accept proof of the existence of surviving souls. On the basis of the batting averages for telepathy, clairvoyance, and psychokinesis reported by him,

this would certainly reduce the communications of such souls to a mute obscurity far below that of the Delphian Oracle and their actions to a numb, poorly directed activity that appears little different from the theory of complete death advanced by the materialists.

It is even more surprising to see that Dr. Rhine feels that recognition of man's dignity depends upon recognition of these vague, hardly perceptible, mute, rather animal or vegetable-like insensate trends and activities that he has taken such pains to demonstrate.

In the end, Dr. Rhine has left the problem where the aborigines and the unsophisticated have had it for centuries.

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SELECTIVE PARTIAL ABLATION OF THE FRONTAL CORTEX; CORRELATIVE STUDY OF ITS EFFECTS ON HUMAN PSYCHOTIC SUBJECTS. Edited by F. A. Mettler. (New York: Paul Hoeber, 1949.)

This is the long-awaited report of the Columbia-Greystone Associates covering a detailed and controlled study of topectomy for mental disorder. Forty-eight patients were selected for intensive study, physical, neurologic, psychiatric, psychologic, biochemical and so on. Half of the patients were operated upon and the other half kept as controls. Three of the control patients were able to live outside the institution a year after selection, and eight of the operated group. Since all the patients were considered well-nigh hopeless as far as spontaneous recovery was concerned, the over-all results of topectomy are encouraging. Four of the 24 operated patients had convulsions.

There is an enormous amount of negative data in the volume. The human individual is evidently able to achieve homeostasis not only in the physiologic field but also in the psychologic, in spite of removal of considerable quantities of his frontal lobes. A battery of 67 psychologic tests yielded no substantial findings as regards intellectual damage attributable to operation. The characteristic and persistent loss had to do with anxiety and the complaint inventory, namely in the affective sphere. Landis states: "No existing theory or hypothesis dealing with the psychologic significance of the human frontal lobe is tenable."

Three of the topectomy patients were later lobotomized with poor outcome. Six control patients were lobotomized, with favorable response in three. Thus it would seem that lobotomy and topectomy are rather similar in their effects. The authors point out, however, that undesirable personality changes are more apt to occur with lobotomy than with topectomy. The important findings of these investigators is that the psychosis is significantly altered when those parts of the frontal lobe termed by Brodmann 9, 10, and 46 are removed. Operations on other parts of the frontal lobe yield little or no change, although one out of three patients with removal of Area 11 responded well. There

was no correlation of improvement with weight of brain removed.

Patients who responded to operation (as well as those who responded without operation) were all endowed with a lively affective response. This is probably the reason for the better result in manic-depressive and involuntal psychotic patients. "Only schizophrenics in whom there is affect appropriate to ideation have a reasonable chance for improvement. . . . Other more conservative types of therapy are sometimes sufficient to arrest the schizophrenic development, but the psychiatrist should always be alert for signs of beginning deterioration so that operation can be undertaken before it is too late. . . . In certain schizophrenics who are in danger of rapid deterioration, the operation is immediately indicated and should replace shock, which is known to be ineffective. Patients of other types who do not respond to shock should not be given one series of treatments after another of a so-called ambulatory type merely to make them more tractable. This frequently leads to extensive damage and masks signs of underlying deterioration. The illness in many of these patients can be markedly shortened by operation."

One more quotation seems worth giving: "We come therefore to this point in the presentation without complete agreement as to just why it has been possible to return a palpable number of apparently incurable psychotic patients to society. The reflective reader will have no reason to regret this state of affairs for it puts him on a par with the present writers."

This work comes at a time when psychosurgery is undergoing very considerable expansion. It is particularly important in revealing that operations upon the frontal lobes, limited to the most anterior portions, can effect a gratifying reduction in psychotic symptomatology, whereas operations in other parts not only do no good but may cause definite harm. Most operations of prefrontal lobotomy are unnecessarily extensive. Selection of patients should be made upon the basis of the affective charge and upon that alone. When the affect dies out, there is no response to any operation. Age, sex, education, occupation, previous attacks and so on are of minor significance. Topectomy is of prime scientific importance, but it is not a method that can be applied on a large scale in state hospitals. Furthermore, the incidence of convulsive seizures (16%) is uncomfortably high. The results of topectomy should prove a new challenge to devise methods of reducing or controlling the activity of Areas 9 and 10 and without the necessity for major surgery.

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**THE ALCOHOLIC WOMAN.** By Benjamin Karpman, M. D. (Washington, D. C.: The Linacre Press, 1948.)

"The Alcoholic Woman" is a contribution toward understanding the causes of alcoholism in a

"certain type of alcoholic woman." In the study of this certain type the author points out factors common to all three patients studied minutely in the book: unsatisfactory childhood environment, persistent feelings of inferiority and insecurity, apparent incestuous interest, suicidal thoughts, and a particular interest in varied sexual outlets. Psychotherapy of these three patients resulted in not particularly optimistic results. This reviewer feels that Dr. Karpman (who has had a wide experience in the field of psychopathology and psychotherapy and reporting his results) concludes that this detailed account of the life histories of these three patients gives one some understanding of the development of this serious symptom-illness, alcoholism. Again, it must be clearly kept in mind when reading the book that each patient with an alcohol problem—whether male or female—is an individual unto himself, and from over 20 years of professional experience this reviewer feels that most of the female patients with alcohol problems do not have all the factors common to the three patients discussed and reported by Dr. Karpman, who is chief psychotherapist of Saint Elizabeths Hospital and clinical professor of psychiatry at Howard University Medical School.

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**THE THIRD MENTAL MEASUREMENTS YEARBOOK.** Edited by Oscar K. Buros. (New Brunswick, N. J.: Rutgers University Press, 1949.)

This volume, as the name implies, is the third in a series of yearbooks designed to present to users of tests in education, industry, psychiatry, and psychology an authoritative and up-to-date bibliography and evaluation of commercially available tests. In spite of the fact that much space is devoted to a discussion of the revisions and the extensions of tests popular in the 20's and 30's, the book is intended to supplement rather than supplant earlier yearbooks in the series. The fact that it covers the period 1940 to 1947, a period which normally would have been covered by 3 or 4 yearbooks, accounts in part for the size of the book.

The book consists of 2 major sections: "Tests and Reviews" (pp. 1-750) and "Books and Reviews" (pp. 751-978). In addition there are 5 indexes and directories: Periodical Directory and Index, Publishers Directory and Index, Index of Titles, Index of Names, and Classified Index of Tests.

The first and perhaps the most important section, entitled "Tests and Reviews," lists 663 tests, 713 original reviews by reviewers, and 3,368 references on the construction, validity, use, and limitations of specific tests. The second part, "Books and Reviews," lists 549 books on measurement and closely related fields and 785 excerpts from reviews of these books in 135 journals.

A book of this kind is exceedingly useful. In addition to providing specific and detailed information it should stimulate authors to standardize and

validate test users interpret

ADDRESS: Rothman

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the study validate tests more adequately, and it should lead test users to exercise caution in the selection and interpretation of their tests.

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ADDRESSES AND PAPERS—1934 TO 1948. By David B. Rotman, M.D. (Psychiatric Institute of the Municipal Court of Chicago, 1948.)

This commemorative volume of selected papers written by the late Dr. David Rotman is an extremely valuable source of reference for all interested in the problems of forensic psychiatry. The unfortunate death of Dr. Rotman prior to publishing a history of his life work in the court setting was indeed a misfortune, and this volume attempts to place in one source of reference many of his papers. His description of the functions of a court psychiatrist can be used very much as a model to all members of the profession who are vitally interested in the part psychiatry can play in assisting the court. He attempts in all his work to impress the need of a psychiatric team. If his attitudes concerning the need of teamwork amongst the disciplines of psychology, psychiatry, and social work could be generally accepted, the psychiatric team would more frequently become a smoothly functioning, well-disciplined unit.

Numerous papers expressing Dr. Rotman's views on alcoholism have been collected in the same volume, and one is constantly impressed by the keen objective analysis that he makes of the problem presented as he sees it from the focus of the municipal court. It is the reviewer's opinion that if Dr. Rotman's philosophies concerning the rôle of psychiatry in a municipal court setting were more widely accepted, it would not be so difficult to affect a liaison between the legal mind and the discipline of medicine. The reviewer would strongly recommend this collection to psychiatrists, psychologists, and social workers whose work in any way falls within the court setting.

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DIE SYNKOPALEN ANFAELLE. Second Edition. By Walter Schulte, M.D. (Stuttgart, Germany: Georg Thieme, 1948.)

This monograph is the second edition of a study that first appeared in 1943. Most of the copies having been destroyed by a bomb, the author revised the manuscript before the second edition was issued. New observations were included and undoubtedly contributed to the excellence of the second edition. It is a closely knit study in which the field of observation became sharply defined and very thoroughly investigated.

The objects of investigation were patients who suffered from habitual syncopal attacks in which definite organic causes coming from cardiac or circulatory, cerebral, allergic, or endocrine disturbances could definitely be excluded. The author succeeded in establishing convincingly differential

diagnostic signs separating the syncopal attack *per se* from those that occur in the course of other diseases such as epilepsy, hysteria, cardiovascular disturbances, narcolepsy, fainting spells in infancy traceable to the sympathetic nervous system, hypoglycemic coma and tetany.

The pathology of the syncopal attack is not, according to the author, based on the dysfunction of a single organ nor a single organ system, but due to psychosomatic factors, whereby the somatic part draws from various components like the organic structure, the sympathetic and central nervous system, as well as the endocrine apparatus.

The first attack is always precipitated by an exogenous element, be it physical overexertion, emotional tension or anxiety.

The author is inclined to accept a hereditary element in the *Bereitschaft*.

The mechanism of the attack is interpreted not only as a sign of deficiency or inferiority of the organism but also as a defense mechanism in the service of the economy of physical and psychic energy. An attempt at therapy and prevention finishes this excellent study.

This monograph offers a great deal of information and new material on a much neglected subject—the ordinary fainting spell in otherwise healthy individuals. It ought to be widely studied by the general practitioner who sees most of such patients first, as well as the specialists in the various fields to whom the patient will be referred later. A good deal of anxiety can be averted in the patient by a correct diagnosis as shown in this study. The material is excellently organized, the sequences well developed and presented with laudable economy of words and a rather impressive logic.

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GUIDING HUMAN MISFITS. By Alexandra Adler, M.D. (New York: Philosophical Library Inc., 1948.)

This second edition of a small volume originally published in 1938 differs from the first primarily by the addition of a chapter on posttraumatic neuroses. The author, daughter of Alfred Adler, presents in nine thoroughly readable chapters the distilled wisdom of a rich clinical experience. The first chapter is a rapid survey of the principles of individual psychology. Other chapters deal with various problems of child psychiatry, neurosis, criminality, dreams, and psychotherapy—based on these principles. At the end of the book is appended "Alfred Adler's questionnaire for the understanding and treatment of problem-children."

The volume is replete with aphorisms to enlarge one's therapeutic arsenal and to aid one's understanding of the "human misfit." Dr. Adler, for example, finds that the stammerer has the habit of "stammering" not only in speech but in other activities." She points out: "The neurotic style represents a 'yes-but' manner of approach. Because of their logic neurotics say 'yes' to the various



tasks which confront them and in saying 'but' they stress all the obstacles preventing them from going ahead. Thus they build up symptom after symptom, behind which they hide. . . ." Very interesting differential characteristics of children occupying the various ordinal positions in their family are given. Throughout the author is mindful of the goal-seeking activity of the patient and directs her operations and thinking accordingly.

This volume is apparently meant as a more or less dogmatic version of the teachings of individual psychology. There is no attempt made to justify the concepts of Adlerian psychology as opposed to Freudian or Jungian. However, acknowledgment is made of the contribution of Freud and in some instances differences in the two schools are indicated. Nevertheless, the reader is disappointed in not finding a critical evaluation here even though Dr. Alexandra Adler intentionally side-steps this issue.

The chapter on dreams and early recollections is probably the weakest in the book. Examples of typical dreams are given and their meanings in terms of goal striving. These meanings in some instances seem forced and one wonders how they were arrived at. It is not too clear to what extent the author uses free association in interpreting dreams.

At times, the distinction between conscious and unconscious seems to be overlooked. Dr. Adler states that people may try to "excuse" their misbehavior by "drives" . . . not realizing that our drives are directed as well as modified in accordance with our individual goal. Everyone experiences at one time or another the most varied types of 'drives' in himself. But fortunately human beings are normally blessed with the ability to choose which drive should be developed and which should be repressed." One might ask, What is the meaning of choice in regard to repression? And is this choice conscious or unconscious?

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THE MENTALLY ILL IN AMERICA. SECOND EDITION.  
By *Albert Deutsch*. (New York: Columbia  
University Press, 1949.)

This book had deservedly wide reading when the first edition was published in 1937, not merely because the author's exhaustive research, therein reported, deserved recognition, but preeminently because the public needed to know the story the book had to tell. The work was reviewed in considerable detail in the July 1937 issue of this JOURNAL.

The present edition traces developments during the intervening 12 years, bringing statistics up to date, describing new treatment methods that have found wide acceptance, setting forth the revised standards for psychiatric hospitals adopted by The American Psychiatric Association in 1945, and including a new chapter, "Psychiatry in World War II."

During the interval between the two editions of this book conditions in the public mental hospitals throughout the country worsened materially in spite of heroic efforts on the part of superintendents and depleted staffs. This deterioration was attributed largely to the effects of war, but matters were made worse by the fact that conditions in many institutions were not good before the war started. This backward state of institutional psychiatry cannot be dissociated from the further fact that the handling and treatment of mental patients has been a not exactly shining demonstration of state medicine in action and inaction. It is opportune, therefore, that the revised edition of Mr. Deutsch's book appears just at this time when the Utopians in and out of government are threatening us with still more state medicine.

Shortly after the end of the war in 1945, Mr. Deutsch started on what he calls "a journalistic survey" of more than two dozen state hospitals from coast to coast. He found deplorable conditions that were shocking enough, but his descriptions sometimes suggest what used to be called "muck raking." When he states: "In some of the wards there were scenes that rivaled the horrors of the Nazi concentration camps," the Editorial Committee felt it necessary to say in a footnote that it "interprets this as figurative language rather than a literal comparison."

Recognition by the federal government that psychiatry is largely state medicine, whether we like it or not, that as such it has not been altogether well conducted and that something ought to be done about it, was given expression in the National Mental Health Act of 1946 authorizing federal grants to aid in training personnel, promotion of research, and augmenting community psychiatric services. This Act the author hails as "probably the greatest single episode in the progress of the mental hygiene movement during the past generation."

As a document in social, medical, and legislative history dealing with the nation's biggest public health problem Mr. Deutsch's book remains an invaluable contribution.

C. B. F.

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